CLINICAL STUDIES REFERENCE GUIDE

October 2017

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## NEW STUDIES

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INTRODUCTION

This document is a list of abstracts of the studies that have been published involving the PhysioFlow technology. Some of them are abstracts of full papers published in peer reviewed journals and some are abstracts of presentations at conventions. They are categorized following the intent of the study (validation, application, or pure research) and also following applications (critical care, cardiology, physiology, etc.). They represent the start of the art about PhysioFlow, to the best of our knowledge.

Some of these studies are quite old and reflect the performance of the technology at an early stage and some are recent and involve our latest innovations (HD-Z motion cancellation filter for instance). Most of the papers are about our PF05-Lab1 design but some recent ones are about the PF07-Enduro, which is newer but offers the same degree of performance.

Also, it is important to note that some teams follow our recommendations strictly and obtain impressive results and some other ones intentionally or unintentionally drift away from our instructions (choice of electrodes, software version, protocol, etc.) and thus generally underperform.

Enjoy your reading and please feel free to contact us should you have questions.
1
VALIDATIONS
1.1 FICK PRINCIPLE/EXERCISE

A New Impedance Cardiograph Device for the Non-invasive Evaluation of Cardiac Output at Rest and During Exercise: Comparison with the "Direct" Fick Method


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Accepted: 3 April 2000

Abstract:
The objectives of this study were to evaluate the reliability and accuracy of a new impedance cardiograph device, the PhysioFlow, at rest and during a steady-state dynamic leg exercise (work intensity ranging from 10 to 50 W) performed in the supine position. We compared cardiac output determined simultaneously by two methods, the PhysioFlow ($\dot{Q}_{\text{PF}}$) and the direct Fick ($\dot{Q}_{\text{Fick}}$) methods. Forty patients referred for right cardiac catheterisation, 14 with sleep apnoea syndrome and 26 with chronic obstructive pulmonary disease, took part in this study. The subjects' oxygen consumption values ranged from 0.14 to 1.19 l · min⁻¹. The mean difference between the two methods ($\dot{Q}_{\text{Fick}} - \dot{Q}_{\text{PF}}$) was 0.04 l · min⁻¹ at rest and 0.29 l · min⁻¹ during exercise. The limits of agreement, defined as mean difference ± 2SD, were -1.34, +1.41 l · min⁻¹ at rest and -2.34, +2.92 l · min⁻¹ during exercise. The difference between the two methods exceeded 20% in only 2.5% of the cases at rest, and 9.3% of the cases during exercise. Thoracic hyperinflation did not alter $\dot{Q}_{\text{PF}}$. We conclude that the Physio Flow provides a clinically acceptable and non-invasive evaluation of cardiac output under these conditions. This new impedance cardiograph device deserves further study using other populations and situations.

Keywords:
• Impedance,
• Cardiography,
• Cardiac output,
• Fick principle,
• Exercise
Non-invasive Cardiac Output Evaluation during a Maximal Progressive Exercise Test, Using a New Impedance Cardiograph Device

DOI 10.1007/s004210100458

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Accepted: 10 April 2001 / Published Online: 4 July 2001

Abstract:
One of the greatest challenges in exercise physiology is to develop a valid, reliable, non-invasive and affordable measurement of cardiac output (CO). The purpose of this study was to evaluate the reproducibility and accuracy of a new impedance cardiograph device, the Physio Flow, during a 1-min step incremental exercise test from rest to maximal peak effort. A group of 12 subjects was evaluated to determine the reproducibility of the method as follows: (1) each subject performed two comparable tests while their CO was measured by impedance cardiography using the new device (COimp1, COimp2), and (2) in a subgroup of 7 subjects CO was also determined by the direct Fick method (COfick) during the second test. The mean difference between the values obtained by impedance (i.e. COimp1-COimp2) was -0.009 l·min⁻¹ (95% confidence interval: -4.2 l·min⁻¹, 4.2 l·min⁻¹), and CO ranged from 3.55 l·min⁻¹ to 26.75 l·min⁻¹ (n=146). When expressed as a percentage, the difference (COimp1-COimp2) did not vary with increasing CO. The correlation coefficient between the values of COimp and COfick obtained during the second exercise test was r=0.94 (P<0.01, n=50). The mean difference expressed as percentage was -2.78% (95% confidence interval: -27.44%, 21.78%). We conclude that COimp provides a clinically acceptable evaluation of CO in healthy subjects during an incremental exercise.

Keywords:
- Impedance,
- Cardiography,
- Cardiac output,
- Maximal exercise test

**Measurements of Cardiac Output during Constant Exercises: Comparison of Two Non-Invasive Techniques**

**Abstract:**
We compared cardiac output (CO) determined simultaneously by electrical impedance cardiography method (COICG) and by the CO2 rebreathing technique (CO2REB) during three different steady-state exercises (target heart rate of 120, 140, and 160 min⁻¹) in 8 healthy fit young men. The mean difference correlation coefficient obtained between the values of COICG and CO2REB was 0.85 and the mean difference (COICG-CO2REB) was 0.06 l/min (0.12 %). At 120 min⁻¹, COICG was lower than CO2REB but the tendency was reversed at 140 and 160 min⁻¹ where COICG was higher than CO2REB. This evolution may be explained by the difficulty of using CO2 rebreathing technique at the highest steady-state exercises and by the progressive acidemia due to exercise. The present results suggest that electrical impedance cardiography method provides acceptable evaluation of CO and may favourably replace the CO2 rebreathing technique during mild (or moderate) to high steady-state exercises.

**Keywords:**
- Impedance,
- Cardiography
- CO2 rebreathing technique,
- Indirect Fick principle,
- Steady state exercise
Does Thoracic Bioimpedance Accurately Determine Cardiac Output in COPD patients during Maximal or Intermittent Exercise?


**Authors:**
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**Study objectives:**
The monitoring of cardiac output (CO) during exercise rehabilitation in patients with COPD, often including strenuous exercise, is advisable. Invasive methods (thermodilution, Fick method) are accurate, but for clinical routine use noninvasive CO estimation is required. We have shown that impedance cardiography (Physio Flow; Manatec Biomedical; Macheren, France) is reliable in COPD patients at rest and during a recumbent, light-intensity exercise. The aim of our study was to evaluate the validity of this noninvasive device in COPD patients during a maximal incremental exercise test (IET) and also during a strenuous intermittent work exercise test (IWET).

**Design:**
Prospective comparative study of the impedance cardiograph vs the direct Fick method applied to oxygen measurements.

**Measurements and main results:**
Forty-nine simultaneous measurements of CO by means of the direct Fick method (CO_f) and CO measured by the impedance cardiograph (CO_pf) were obtained during the IET, and 108 measurements were made during the IWET. The correlation coefficients between the two measurements were \( r = 0.85 \) and \( r = 0.71 \) for the IET and the IWET, respectively. \( CO_pf \) was higher than \( CO_f \). The difference between the two methods was 3.2 +/- 2.9 L/min during the IET and 2.5 +/- 2.1 L/min during the IWET. Expressed as a percentage of the mean of the two measurements, this corresponded to 31 +/- 21% and 25 +/- 20%, respectively.

**Patients:**
Eight patients with moderate-to-severe COPD (59 +/- 6 years old; FEV(1), 38 +/- 15% predicted; residual volume, 194 +/- 64% predicted) [mean +/- SD].

**Conclusion:**
The relatively high number of values differing by > 20% precludes the use of impedance cardiography in clinical routine in such a difficult setting (hyperinflated patients and intense exercise).

**IMPORTANT NOTE FROM THE MANUFACTURER:**
In an effort to present all publications involving PhysioFlow we have decided to include this particular one in our list. Its results may not look as favourable as all the other abstracts. However, it is to be noted that the protocol was performed in a way that is not compliant with the manufacturer’s instructions: The investigators have used a particular prototype version of the PhysioFlow software in spite of our insistence that they should not do so. They have used electrodes that were not those recommended for optimal results. Moreover, data of this study have disappeared from the hard disk of the computer, making it impossible to reanalyse them with the appropriate version of the software. In addition, it is questionable that the Fick would perform well under incremental or strenuous intermittent work exercise test.
Reliability of Peak VO(2) and Maximal Cardiac Output Assessed using Thoracic Bioimpedance in Children


Authors:
- Welsman J,
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- Welford D,
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Abstract:
The purpose of this study was to evaluate the reliability of a thoracic electrical bioimpedance based device (PhysioFlow) for the determination of cardiac output and stroke volume during exercise at peak oxygen uptake (peak VO(2)) in children. The reliability of peak VO(2) is also reported. Eleven boys and nine girls aged 10-11 years completed a cycle ergometer test to voluntary exhaustion on three occasions each 1 week apart. Peak VO(2) was determined and cardiac output and stroke volume at peak VO(2) were measured using a thoracic bioelectrical impedance device (PhysioFlow). The reliability of peak VO(2) cardiac output and stroke volume were determined initially from pairwise comparisons and subsequently across all three trials analysed together through calculation of typical error and intraclass correlation. The pairwise comparisons revealed no consistent bias across tests for all three measures and there was no evidence of non-uniform errors (heteroscedasticity). When three trials were analysed together typical error expressed as a coefficient of variation was 4.1% for peak VO(2) 9.3% for cardiac output and 9.3% for stroke volume. Results analysed by sex revealed no consistent differences. The PhysioFlow method allows non-invasive, beat-to-beat determination of cardiac output and stroke volume which is feasible for measurements during maximal exercise in children. The reliability of the PhysioFlow falls between that demonstrated for Doppler echocardiography (5%) and CO(2) rebreathing (12%) at maximal exercise but combines the significant advantages of portability, lower expense and requires less technical expertise to obtain reliable results.
Does Advanced Cardiac Impedance Technology Accurately Measure Cardiac Output During Submaximal Steady State Exercise?

Control/Tracking Number: 09-SA-3991-ACSM

Activity: Scientific Abstract

Current Date/Time: 11/3/2008 8:13:33 PM

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Abstract:
This study determined if advanced cardiac impedance technology (ACI) could accurately measure cardiac output during steady-state cycling exercise compared to values calculated using the direct Fick equation developed by Stringer et al (1997). METHOD: VO2 max was determined on both a treadmill (Mean = 3.96 ± 1.2 liters/min) and cycle ergometer (Mean = 3.42 ± 1.2 liters/min) in 15 subjects (Age; 34.3. ± 9.4 yrs). Steady-state exercise wattage was set at 25%, 50%, and 75% of peak watts achieved. Subjects exercised 8 mins at each stage. The last 4 mins were used to determine the ACI values for cardiac output (Q), heart rate, stroke volume, EDV, SBP, DBP, and systemic vascular resistance. Both the submaximal and maximal exercise trials were performed in duplicate to assure accurate data collection. No significant differences were observed in test-retest trials. Thus, the mean of duplicate trials was used for all data analyses.

Keywords:
- Cardiac impedance,
- Steady state exercise
- Cycle ergometry

Category:
204 acute exercise

Author Disclosure Information:
C.E. Broeder, PhysioFlow Corporation, Contracted Research.

Results:
There was no significant difference between the cardiac output determined by the Stringer equation and the ACI measured Q value. The percent differences across exercise intensity’s for Q were 4.2%, -1.5%, and -6.7% for the 25%, 50%, and 75% of max watts, respectively. Linear regression analyses indicated r squared = 0.99, SEE = 0.20 liters, p = .001. For all trials combined, the mean percent difference between the stringer cardiac output and the ACI cardiac output was 0.5%.

<table>
<thead>
<tr>
<th>STAGE INTENSITY</th>
<th>VO2 % OF VO2 MAX</th>
<th>A-V DO2</th>
<th>STRINGER Q</th>
<th>ACI Q</th>
<th>% DIFFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>25% MAX WATTS</td>
<td>1.37 40.1</td>
<td>0.097258</td>
<td>14.1</td>
<td>13.5</td>
<td>4.2%</td>
</tr>
<tr>
<td>50% MAX WATTS</td>
<td>2.17 63.5</td>
<td>0.120650</td>
<td>18.0</td>
<td>18.3</td>
<td>-1.5%</td>
</tr>
<tr>
<td>75% MAX WATTS</td>
<td>3.02 88.3</td>
<td>0.145504</td>
<td>20.8</td>
<td>22.2</td>
<td>-5.7%</td>
</tr>
<tr>
<td>MEAN OF ALL TRIALS</td>
<td>2.19 63.9</td>
<td>0.121138</td>
<td>18.1</td>
<td>17.97</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

Conclusion:
In conclusion, these data indicate that the ACI system used in this study was highly accurate in determining a person’s Q during steady state exercise ranging between 40.1% and 88.3% of VO2 max. Future studies need to determine if similar accuracy can be achieved using other forms of exercise, i.e., treadmill.
The Ergogenic Effect of Recombinant Human Erythropoietin on VO2max Depends on the Severity of Arterial Hypoxemia

Citation:

Editor:
Timothy Secomb, University of Arizona, United States of America

Funding:
This study was supported by research fundings from Anti Doping Danmark (Denmark), Kulturministeriet (Denmark) and Bundesamt für Sport (Switzerland) to C.L. This study was also supported in part by research funding from Gobierno de Canarias (Ayudas para estancias postdoctorales)(Spain) to J.A.L.C. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests:
The authors have declared that no competing interests exist.

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Received May 6, 2008; Accepted July 28, 2008; Published August 20, 2008

Abstract:
Treatment with recombinant human erythropoietin (rhEpo) induces a rise in blood oxygen-carrying capacity (CaO2) that unequivocally enhances maximal oxygen uptake (V’O2max) during exercise in normoxia, but not when exercise is carried out in severe acute hypoxia. This implies that there should be a threshold altitude at which V’O2max is less dependent on CaO2.

To ascertain which are the mechanisms explaining the interactions between hypoxia, CaO2 and V’O2max we measured systemic and leg O2 transport and utilization during incremental exercise to exhaustion in normoxia and with different degrees of acute hypoxia in eight rhEpo-treated subjects. Following prolonged rhEpo treatment, the gain in systemic VO2max observed in normoxia (6–7%) persisted during mild hypoxia (8% at inspired O2 fraction (FIO2) of 0.173) and was even larger during moderate hypoxia (14–17% at FIO2 = 0.153–0.134). When hypoxia was further augmented to FIO2 = 0.115, there was no rhEpo-induced enhancement of systemic V’O2max or peak leg V’O2. The mechanism highlighted by our data is that besides its strong influence on CaO2, rhEpo was found to enhance leg V’O2max in normoxia through a preferential redistribution of cardiac output toward the exercising legs, whereas this advantageous effect disappeared during severe hypoxia, leaving augmented CaO2 alone insufficient for improving peak leg O2 delivery and V’O2. Finally, that V’O2max was largely dependent on CaO2 during moderate hypoxia but became abruptly CaO2-independent by slightly increasing the severity of hypoxia could be an indirect evidence of the appearance of central fatigue.

Agreement between impedance and dye dilution for cardiac output measurement:

This graph shows the agreement (Bland-Altman plot) between the cardiac impedance technique and the indocyanine green dye dilution method for measuring cardiac output during exercise obtained from 55 measurements in seven subjects. For each measurement, the difference between the two methods is plotted against the average of both techniques. The solid line indicates the mean bias, while the dotted lines indicate the 95% confidence intervals (2×standard deviation).
Poor accuracy of noninvasive cardiac output monitoring using bioimpedance cardiography [PhysioFlow(R)] compared to magnetic resonance imaging in pediatric patients

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Abstract: Identification of low cardiac output (CO) states in anesthesia is important because preoperative hemodynamic optimization may improve outcome in surgery. Accurate real-time CO measurement would be useful in optimizing "goal-directed" therapy. We sought to evaluate the reliability and accuracy of CO measurement using bioimpedance cardiography (PhysioFlow®, NeuMeDx, Bristol, PA) in pediatric patients with and without cardiac disease undergoing anesthesia for magnetic resonance imaging (MRI).

Methods: All consenting patients undergoing anesthesia for cardiac MRI were enrolled. After equilibration of anesthesia for ≥10 minutes, 6 PhysioFlow electrodes were applied to the patient’s chest for continuous real-time monitoring for 10 minutes. Data were stored in 15-second epochs and later averaged offline to obtain CO. Phase contrast MRI measurements of flow volumes in the superior vena cava and ascending and descending aorta were made from a single imaging plane through all 3 vessels at the level of the right pulmonary artery. Both CO measurements were indexed to body surface area. The anesthetic technique was the same for both measurements. Agreement was assessed using Bland-Altman analysis.

Results: Thirty-one patients were enrolled and 23 were analysed. The median age at study was 2.8 years (range, 0.02-8.02 years) and median body surface area was 0.54 m(2) (range, 0.21-1.00 m(2)). Eleven of the 23 patients (48%) were males. Patients were grouped into those with univentricular physiology, 6 of 23 (26%); biventricular physiology with shunt, 3 of 23 (13%); biventricular without shunt, 10 of 23 (43%); and no structural heart disease, 4 of 23 (17%). The mean bias was -0.34 ± 1.50 L/min/m(2) (P = 0.29). The 95% limits of agreement were -3.21 to +2.69 L/min/m(2). Only 8 of 23 measurements (35%) were within 20% and 14 of 23 measurements (61%) were within 30% of each other.

Conclusion: PhysioFlow performance was not sufficiently accurate in this population. Modifications of the algorithm and further testing are required before this device can be recommended for routine clinical use in pediatric patient.

IMPORTANT NOTE FROM THE MANUFACTURER:
We do respect the Toronto Sick Children hospital team for their friendliness and professionalism. However there was a technical mistake in their data manipulation and all PhysioFlow recordings were lost by the research team before we could take a look at it and see what happened. Please bear in mind that it was the very first time our system was applied to such a patient population and it was never calibrated for it before. It would have been extremely helpful to access the PhysioFlow recordings to
1) Assess their quality and potential operator’s mistakes
2) Reprocess them with newer algorithms we developed later (these ones date back to 2004)
3) Calibrate the system to adapt it to this patient population.
This was the initial plan but it could never be implemented because of the loss of data.
Evaluation of Impedance Cardiography for Measurement of Stroke Volume in Congenital Heart Disease.

PMID: 27562130 DOI: 10.1007/s00246-016-1456-x

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Abstract:
Noninvasive measurement of cardiac output (CO) and particularly stroke volume (SV) remain difficult but potentially valuable. These variables can be particularly challenging to measure in children with congenital heart disease (CHD). Impedance cardiography (IC) is a technique shown to be accurate in measuring SV in adults and in children with structurally normal hearts. The ease of use and rapidity of SV measurement using IC makes it potentially attractive for young patients with CHD. Advances in IC technology have led to more sophisticated signal-morphology IC (SMIC) devices that may further improve accuracy. We tested the accuracy of SMIC to measure SV in 21 subjects with CHD by comparing measurements with those from cardiac magnetic resonance (CMR) imaging. There was good agreement between SMIC and CMR in measurement of SV: mean difference = 1.7 ml (p = 0.47); r = 0.89. The agreement and correlation persisted when controlling for the differences in blood pressure and heart rate during the two testing methods. We conclude that SMIC is accurate at measuring SV and thus CO when compared to CMR in a variety of forms of CHD.

Keywords:
- Cardiac output;
- Congenital heart disease;
- Impedance cardiography;
- Stroke volume

IMPORTANT NOTE FROM THE MANUFACTURER:
This positive article confirms that the previous one contained severe methodological errors.
Evaluation of two methods for continuous cardiac output assessment during exercise in chronic heart failure patients


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Abstract:

The purpose of this study was to evaluate the accuracy of two techniques for the continuous assessment of cardiac output in patients with chronic heart failure (CHF): a radial artery pulse contour analysis method that uses an indicator dilution method for calibration (LiDCO) and an impedance cardiography technique (Physioflow), using the Fick method as a reference. Ten male CHF patients (New York Heart Association class II–III) were included. At rest, cardiac output values obtained by LiDCO and Physioflow were compared with those of the direct Fick method. During exercise, the continuous Fick method was used as a reference. Exercise, performed on a cycle ergometer in upright position, consisted of two constant-load tests at 30% and 80% of the ventilatory threshold and a symptom-limited maximal test. Both at rest and during exercise LiDCO showed good agreement with reference values [bias ± limits of agreement (LOA), −1% ± 28% and 2% ± 28%, respectively]. In contrast, Physioflow overestimated reference values both at rest and during exercise (bias ± LOA, 48% ± 60% and 48% ± 52%, respectively). Exercise-related within-patient changes of cardiac output, expressed as a percent change, showed for both techniques clinically acceptable agreement with reference values (bias ± LOA, 2% ± 26% for LiDCO, and −2% ± 36% for Physioflow, respectively). In conclusion, although the limits of agreement with the Fick method are pretty broad, LiDCO provides accurate measurements of cardiac output during rest and exercise in CHF patients. Although Physioflow overestimates cardiac output, this method may still be useful to estimate relative changes during exercise.

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Cardiac output during exercise: A comparison of four methods

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Abstract:

Several techniques assessing cardiac output (Q) during exercise are available. The extent to which the measurements obtained from each respective technique compares to one another, however, is unclear. We quantified Q simultaneously using four methods: the Fick method with blood obtained from the right atrium (QFick-M), Innocor (inert gas rebreathing; QInn), Physioflow (impedance cardiography; QPhys), and Nexfin (pulse contour analysis; QPulse) in 12 male subjects during incremental cycling exercise to exhaustion in normoxia and hypoxia (FiO₂ = 12%). While all four methods reported a progressive increase in Q with exercise intensity, the slopes of the Q/oxygen uptake (VO₂) relationship differed by up to 50% between methods in both normoxia [4.9 ± 0.3, 3.9 ± 0.2, 6.0 ± 0.4, 4.8 ± 0.2 L/min per L/min (mean ± SE) for QFick-M, QInn, QPhys and QPulse, respectively; P = 0.001] and hypoxia (7.2 ± 0.7, 4.9 ± 0.5, 6.4 ± 0.8 and 5.1 ± 0.4 L/min per L/min; P = 0.04). In hypoxia, the increase in the Q/VO₂ slope was not detected by Nexfin. In normoxia, Q increases by 5–6 L/min per L/min increase in VO₂, which is within the 95% confidence interval of the Q/VO₂ slopes determined by the modified Fick method, Physioflow, and Nexfin apparatus while Innocor provided a lower value, potentially reflecting recirculation of the test gas into the pulmonary circulation. Thus, determination of Q during exercise depends significantly on the applied method.

IMPORTANT NOTE FROM THE MANUFACTURER:

The research team, contacted for the first time after publication, did not wish to share details about the software version that was used (which is important regarding the filtering of signals), nor the skin preparation methodology/electrode type. However they found that PhysioFlow generates fewer impossible /implausible readings than other methods.

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Comparison of Thoracic Bioimpedance with Acetylene Uptake for Measuring Cardiac Output.


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Abstract:
Cardiac output is shown to be a key determinant for oxygen transport, performance and health. Reliable and accurate non-invasive measurements of cardiac output, especially during exercise, are therefore of importance. The present study compared a new thoracic bioimpedance method with the established single-breath acetylene uptake method. We assessed cardiac output in 20 (24±4 years) moderately trained males, at rest and during cycling. Both methods showed good test-retest reliabilities with ±2 SD limits of agreement of 3.67 and -4.50 L·min⁻¹ (thoracic bioimpedance) and 4.46 and -5.69 L·min⁻¹ (single breath), respectively. When thoracic bioimpedance was compared with single breath, the ±2 SD limits of agreement were poor (-6.05 and 9.57 L·min⁻¹). Thoracic bioimpedance displayed significantly lower (p<0.05) absolute cardiac output values than single breath, and the cardiac output-oxygen consumption slopes (y=5.7x+5.5 (single breath) and y=5.0x+5.0 (thoracic bioimpedance) tended (p=0.08) to show less increase for thoracic bioimpedance. Conclusions: Results from the single-breath method are in line with previous findings, showing a good reliability. Although thoracic bioimpedance showed a similar reliability as the single-breath method, and is easier to use, the agreement with single breath was poor, and thoracic bioimpedance seems not to be able to replace it.

IMPORTANT NOTE FROM THE MANUFACTURER:
The Enduro unit on loan in Trondheim was an early stage device and had a defective ECG detection in the firmware, which has been corrected in the meantime. It resulted in a poor calculation of HR and also a bad trigger for the signal stabilization filter. We were offered the opportunity to reprocess the data. Unfortunately the team did not maintain the patients at real rest after calibration and therefore re-calculating the calibration and the test was not productive. This study should not have been published without mention of these issues as they affect its entire validity.

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PMID: 24886928 [PubMed - as supplied by publisher]
1. Validations

1.1 Fick Principle/Exercise

Reliability of exercise cardiac output measurement in COPD using impedancemetry: comparison with CO2 and inert gas rebreathing.

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Rationale:
The interest in the measurement of exercise cardiac output (Qc) in patients with Chronic Obstructive Pulmonary Disease (COPD) has resurfaced due to the recent proposition that dynamic hyperinflation may result in blood trapping within the pulmonary circulation, thereby limiting oxygen delivery and exercise capacity. To date, the ability to measure Qc non-invasively in these patients is constrained by techniques dependent upon appropriate ventilation: perfusion for adequate pulmonary blood-gas diffusion. The technique of thoracic bioimpedance presents an interesting alternative as it does not depend on gas lung transfer factors, provides continuous measurement from rest to peak exercise and is free of patient interaction, unlike rebreathing methods. This study reports on the reliability of thoracic bioimpedance (Physioflow®) compared to standard CO2-rebreathing and inert-gas rebreathing (Innocor®) techniques for use in test-retest submaximal steady state exercise.

Methods:
Stable COPD patients (N=8; 66±4 yrs; FEV1= 56±6% pred.) were assessed on 2 occasions separated by at least 2 days. Qc was measured using the 3 techniques at the end of 5-minute steady-state cycling at 20, 35, 50 and 65% peak power bouts. The reported Qc was the average of 2 consecutive measures at each workload.

Results:
All techniques provided measurements in a physiologically acceptable range for the power output and showed good reproducibility with no difference in test-retest mean values. CO2 rebreathing resulted in systematically higher values both at rest and during exercise as compared to Physioflow® (mean Δ L/min: 0.5 rest; 0.7, 0.3, 0.8 at 20, 35, 50% peak power). In contrast, Innocor® resulted in systematically lower rest and exercise values as compared to Physioflow® (mean Δ L/min: 1.6 rest; 1.6, 1.2, 1.8 at 20, 35, 50% peak power). Results also showed the coefficient of reproducibility calculated on test-retest to be highest in Physioflow® (R2 = 0.80) compared with Innocor® and CO2 rebreathing (R2 = 0.72 and 0.53).

Conclusion:
These preliminary results suggest that thoracic bioimpedance presents a valuable tool to monitor Qc in COPD under resting and moderate exercise conditions resulting in significant hyperventilation and moderate dynamic hyperinflation.

Funded by: Respiratory and Epidemiology Clinical Research Unit of the McGill University Health Center
1. Validations
1.2 Thermodilution/Echo-Doppler/Rest

1.2 THERMODILUTION/ECHO-DOPPLER/REST

Cardiac Output Measurements: Comparison between a New Transthoracic Electrical Bioimpedance Method (Physioflow™) and the Swan-Ganz Method (Continuous Cardiac Output or Bolus Technique)

Published at the French Anaesthesiology Society, Sept 2001

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Abstract:
Cardiac Output (CO) measurement using Transthoracic Electrical Bioimpedance (TEB) has been recently improved. We have tested a system using exclusively relative values of the impedance signal, and not absolute values (Z0). Indeed, the Z0 value has been described as being at origin of the practical limitations of TEB. We have chosen the Swan-Ganz method to provide reference values, using boluses (B), or continuous cardiac output (CCO) (BAXTER™ Vigilance®).

Results:
107 ICU patients underwent simultaneous CO measurements using the two methods (CO Swan Ganz: 20 B and 87 CCO). One measurement was performed on every patient (84 Male/23 Female, age 69±11 years, weight 75±15 Kg, height 167±8 cm). Pathologies: aortic and bypass surgery 65 %, septic shock 18%, heart failure 7%, pulmonary patients 7%, misc. 3%. Linear regression factor was 0.88 (p<0.001). CO PhysioFlow = 0.75 CO Swan + 1.33. Bland and Altman diagram is represented below (bias = -0.014 L/min).

Conclusion:
This study has been done under the most difficult conditions for TEB: one single measurement per patient, and patients presenting a very large variety of pathologies. This new TEB method deserves further investigations, using the Fick method, on the same range of unselected ICU patients. Indeed, literature displays that Fick as a reference method features a reduced dispersion of results compared to thermodilution

References:
Conclusion of the report on PhysioFlow Studies performed at MUSC Charleston, SC and UPMC Pittsburgh, PA, 2007

This multicenter study has been performed on a population of representative American patients referred to major medical institutions for severe cardiovascular diseases. In that frame PhysioFlow has proven that it is substantially equivalent to the predicate device (Philips) and FDA should grant clearance because:

It performs much better that the predicate device in terms of accuracy and ability to provide clinically relevant numbers, even in difficult patients. Its comparative measurements to a clinically accepted reference method are as good as expected with reference to the best scientific literature. It performs as well as the best established invasive reference technique (Fick) with comparison to thermodilution

In conclusion, this study achieved its objective of demonstrating

1) The agreement in CO between the PhysioFlow ICG PF-05 and thermodilution is similar to or better than the agreement between the Philips ICG and thermodilution; and
2) Absolute agreement between the PhysioFlow ICG PF-5 itself and thermodilution is adequate when accounting for the known variability in the thermodilution reference method.
Purpose:
To assess impedance cardiography as a method for obtaining a non-invasive hemodynamic evaluation in patients with pulmonary hypertension (PH).

Methods:
A total of 39 patients (age 57±14 years, 87% women) with presumed (23%) or confirmed PH (77%) of different etiologies who underwent right heart catheterization (RHC) at University of Florida from August 2009 to March 2010 agreed to be studied by impedance cardiography (PhysioFlow(r) PF-05, Manatec Biomedical, Macheren, France) immediately after RHC. PhysioFlow(r) measures cardiac output (CO) and end-diastolic volume (EDV), among other parameters.

Results:
The median pulmonary artery pressure was 36 (IQR 26-56) mm Hg. The CO (mean ± SD in l/min) by thermodilution (CO-T), Fick methodology (CO-F) and impedance cardiography (CO-IC) was 5.9 ± 2.2, 5.5 ± 1.6 and 5.6 ± 1.5, respectively. Bland-Altman analysis of CO-T versus CO-F showed mean of 0.4 L/min (95% limit of agreement (LoA) 3.4 and -2.6), CO-T versus CO-IC a mean of 0.3 L/min (95% LoA 2.8 and -2.2) and CO-F versus CO-IC a mean of -0.1 L/min (95% LoA 2.5 and -2.7). Correlation between CO-T and CO-IC was R² = 0.7, p < 0.001. In patients with PH the correlation of CO-T and CO-IC had a mean of 0.4 L/min (95% LoA 2.9 and -2.2), R² = 0.75, p < 0.001. Pulmonary artery occlusion pressure (PAOP) correlated with EDV (R² = 0.2, p = 0.005). By ROC analysis EDV of 200 ml had a sensitivity of 53% and a specificity of 86% for PAOP > 15 mm Hg (AUC: 0.78).

Clinical Implications:
Impedance cardiography reliably measures cardiac output in patients with pulmonary hypertension. This methodology may serve as a valid tool for the hemodynamic evaluation of this group of patients.

Conclusion:
Impedance cardiography allows a reliable and non-invasive measurement of cardiac output in patients with PH. End-diastolic volume correlated with pulmonary artery occlusion pressure.

Disclosure:
Adriano Tonelli, No Financial Disclosure Information; No Product/Research Disclosure Information
Value of Impedance Cardiography in Patients Studied for Pulmonary Hypertension

Pulmonary Hypertension Posters
24 May, 2011

Authors:
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• Robin Carrie,
• Kamal K. Mubarak

Abstract:
The aim of this study was to evaluate the accuracy and precision of impedance cardiography as a method for noninvasive hemodynamic evaluation of patients with pulmonary hypertension (PH). We performed a prospective and blinded study of patients who underwent right heart catheterization (RHC) for evaluation of known or presumed PH at the University of Florida from August 2009 to March 2010. The cohort consisted of a total of 39 patients (age = 57 ± 14 years, 87% women) with presumed (23%) or confirmed PH (77%) of different etiologies. Patients underwent RHC and impedance cardiography using the PhysioFlow PF-05.

The PhysioFlow PF-05 measures cardiac output (CO) and LV end-diastolic volume (LVEDV), among other parameters. The median pulmonary artery pressure was 36 (IQR 26-56) mmHg. The CO (mean ± SD) by thermodilution (CO-T) and by impedance cardiography (CO-IC) was 5.9 ± 2.2 and 5.6 ± 1.5 L/min, respectively. Bland-Altman analysis of CO-T versus CO-IC revealed a mean of 0.3 L/min (95% LoA: -2.2 to 2.8). In patients with PH, the correlation of CO-T and CO-IC had a mean of 0.4 L/min (95% LoA: 2.9 and -2.2). Pulmonary artery occlusion pressure (PAOP) correlated with LVEDV (R² = 0.2, p = 0.005). By ROC analysis, EDV C 200 ml had a sensitivity of 53% and a specificity of 86% for PAOP[15 mmHg (AUC = 0.78). In patients with PH, impedance cardiography had good accuracy and fair precision for CO determination when compared with thermodilution. Impedance cardiography may provide information about the preload status and has the potential to become a cost-effective and noninvasive method for the follow-up of patients with PH.
The PhysioFlow Thoracic Impedancemeter Is Not Valid for the Measurements of Cardiac Hemodynamic Parameters in Chronic Anemic Patients

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• Cyrille Serges Dah

Abstract:
The aim of the present study was to test the validity of the transthoracic electrical bioimpedance method PhysioFlow® to measure stroke volume in patients with chronic anemia. Stroke volume index (SVI), as well as cardiac index (CI) obtained by transthoracic electrical bioimpedance method and doppler echocardiography were compared in healthy subjects (n = 25) and patients with chronic anemia (i.e. mainly with sickle cell anemia; n = 32), at rest. While doppler echocardiography was able to detect difference in SVI between the two populations, the Physioflow® failed to detect any difference. Bland & Altman analyses have demonstrated no interchangeability between the two methods to assess CI and SVI in anemic patients and healthy subjects. While doppler echocardiography displayed a good concordance for SVI results with those obtained in the literature for anemic patients, the Physioflow® did not. Finally, in contrast to doppler echocardiography:

1) the CI obtained with the Physioflow® was not correlated with the hemoglobin level and
2) the stroke volume determined by the Physioflow® was highly influenced by body surface area. In conclusion, our findings indicate that the Physioflow® device is inaccurate for the measurement of SVI and CI in patients with chronic anemia and has a poor accuracy for the measurement of these parameters in African healthy subjects.

IMPORTANT NOTE FROM THE MANUFACTURER:
This is an absurd outcome generated by a very early development software that should never have been used by any customer and was unfortunately released by mistake to one center in France and passed on to this center in Abidjan. In truth, PhysioFlow SVi is NOT correlated to body height or weight.

The research team, contacted for the first time after publication, did not wish to share details about the software version that was used nor accepted our offer to reprocess recordings with the appropriate version of the software, which is highly regrettable.
There is absolutely no evidence precluding the use of PhysioFlow in the African population.
Stroke Volume Variation Measured by Impedance Cardiography During Passive Leg Raising to Assess Fluid Responsiveness After Cardiac Surgery

Abstract:
After cardiac surgery, fluid management is critical and has a major impact on morbidity and mortality. A reliable parameter to predict fluid responsiveness is essential. The aim of this study was to investigate whether the measure of stroke volume variations (ΔSV) by impedance cardiography during passive leg raising (PLR) can reliably predict preload dependency after cardiac surgery, in comparison to a reference parameter: velocity time integral variation (ΔVTI) measured by transthoracical echocardiography (TTE).

Material and methods:
A prospective, observational study was conducted after obtaining ethics committee approval and informed consent, on patients requiring cardiac surgery with extracorporeal circulation. The PLR maneuver was performed within the two first hours after surgery on sedated patients under mechanical ventilation and with sinus rhythm. All hemodynamic variables (heart rate, systolic and diastolic arterial pressure, central venous pressure (CVP), left auricular pressure (LAP), SV, VTI, cardiac output and index, left ventricular filling pressures (LVFP), ejection fraction) were measured before and after PLR.

We classified patients as responders (R) or non responders (NR): R were defined as patients presenting a ΔVTI ≥ 12 % during the 90 seconds following PLR, and NR as patients presenting a ΔVTI < 12 %.

The ΔSV measured by impedance cardiography was compared to the ΔVTI. The area under the ROC curve was determined to assess the ability of ΔSV to classify the R and NR patients.

Secondary aims of the study were to search for other predictive parameters for preload dependence: CVP, LAP and LVFP variations after PLR and respiratory variations of inferior vena cava. Patients were otherwise treated according to the regular protocol of the ICU. The physicians of the ICU were blinded to impedance cardiography measures.

Results:
Among the 50 included patients, 24 were R (48%) and 26 NR (52%).

The area under the ROC curve was 0.818 (p = 0.0008). A ΔSV ≥ 20.7 % allowed discrimination between R and NR with a sensitivity of 86.2 % and a specificity of 90.5 %.

We didn’t find any other significantly predictive parameter for preload dependency.

Conclusion:
Based on the comparison to ΔVTI measured by TTE, ΔSV measured by impedance cardiography during a PLR maneuver seems to be a reliable predictor for preload dependency after cardiac surgery.
Validation of impedance cardiography in pulmonary arterial hypertension

Clinical Physiology and Functional Imaging 2017 February 6

**Authors:**

- Marios Panagiotou,
- Ioannis Vogiatzis,
- Geeshath Jayasekera,
- Zafeiris Louvaris,
- Alison Mackenzie,
- Neil Mcglinchey,
- Julien S Baker,
- Alistair C Church,
- Andrew J Peacock,
- Martin K Johnson

**Background:**

Non-invasive methods of measuring cardiac output are highly desirable in pulmonary arterial hypertension (PAH). We therefore sought to validate impedance cardiography (ICG) against thermodilution (TD) and cardiac magnetic resonance (CMR) in the measurement of cardiac output in patients under investigation for PAH.

**Methods:**

A prospective, cross-sectional study was performed to compare single-point measurements of cardiac output obtained by impedance cardiography (COICG) technology (PhysioFlow®) with (i) contemporaneous TD measurements (COTD) at rest and steady-state exercise during right heart catheterization and (ii) CMR measurements (COCMR) at rest obtained within 72 h.

**Results:**

Paired COICG and COTD measurements were obtained in 25 subjects at rest and 16 subjects at exercise. COCMR measurements were obtained in 16 subjects at rest. There was unsatisfactory correlation and agreement between COICG and COTD at rest ($r = 0.42$, $P = 0.035$; bias: $1.21 \text{ l min}^{-1}$, 95% CI: $-2.33$ to $4.75 \text{ l min}^{-1}$) and exercise ($r = 0.65$, $P = 0.007$; bias: $1.41 \text{ l min}^{-1}$; 95% CI: $-3.99$ to $6.81 \text{ l min}^{-1}$) and in the change in COICG and COTD from rest to exercise ($r = 0.53$, $P = 0.033$; bias: $0.76 \text{ l min}^{-1}$, 95% CI: $-3.74$ to $5.26 \text{ l min}^{-1}$). There was also a lack of correlation and unsatisfactory agreement between resting COICG and COCMR ($r = 0.38$, $P = 0.1$; bias: $1.40 \text{ l min}^{-1}$; 95% CI: $-3.48$ to $5.28 \text{ l min}^{-1}$). In contrast, there was close correlation and agreement between resting COTD and COCMR ($r = 0.87$, $P<0.001$; bias: $0.16 \text{ l min}^{-1}$, 95% CI: $-1.97$ to $1.65$).

**Conclusion:**

In a representative population of patients under investigation for PAH, ICG showed insufficient qualitative and quantitative value in the measurement of resting and exercise cardiac output when compared with TD and CMR.

**IMPORTANT NOTE FROM THE MANUFACTURER:**

This study was performed with an older generation PhysioFlow Enduro which was equipped with a built-in amplifier that was underperforming in such "difficult" patient population. The study below shows good performance in a similar population, with an upgraded device featuring the current amplifier.
Accuracy of impedance cardiography to measure cardiac output at rest in pulmonary hypertension


Authors:
• Elise Noel-Savina,
• Laurent Tetu,
• Grégoire Prévot,
• Marion Dupuis,
• Fabien Pillard,
• Daniel Rivière,
• Alain Didier

Abstract:

Introduction: Cardiac output (CO) is one of the most important prognostic factor in PH and is required for the assessment of treatment response. CO is measured invasively by right heart catheterization by thermodilution or the Fick method. Impedance cardiography (IP) measures CO and is noninvasive, simple and provides immediate results.

Objectives: The main objective of this feasibility study was to assess the accuracy of of CO measures performed IP compared to the Fick method in selected patients treated for PH (Group 1 or 4). Secondary objectives were to evaluate the accuracy of CO evaluation by IP compared to thermodilution and to determine the factors that may affect the measures.

Methods: Patients were recruited from the cohort of the Competence Center PH of Midi-Pyrenees, France. The three techniques (Fick, thermodilution and IP) were realized at the same time during right heart catheterization performed in the patient follow up. All patients had confirmed PH from Group 1 or group 4.

Results: We had recruited 37 subjects in the study. (31 patients group 1 and 6 patients group 4). The CO measured by IP correlates with the CO measured by the Fick method: ρ=0.62 CI 95% [0.3064; 0.8124] (P<0.001) and ρ²= 0.385. The CO measured by IP correlates with the CO measured by thermodilution: p=0.7468 CI 95% [0.5578; 0.8622] (p<0.0001) and p²= 0.56. In PH patients CO changes observed during the test was related to stroke volume variation and predominantly in patients known to have intracardiac shunt.

Conclusion:
This pilot study validates the measurement of CO by IP in patients with PH (group 1 or 4). This suggests a potential role of the non-invasive IP in the follow up of PH patients.

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1. Validations
1.3 Reproducibility/Electrode Placement

Measurement of Cardiac Output Using PhysioFlow® with Different Positions of Electrode Placement

*Singapore Med J 2006; 47(11): 967*

**Authors:**
- Tan K H,
- Lai F O,
- Hwang N C

**Abstract:**
PhysioFlow is a non-invasive impedance cardiograph device that measures cardiac output. Recommended electrode placements involve six electrodes, including two near the xiphisternum (Z3 and Z4/EcG3/neutral). This study aims to evaluate if changing the positions of these two leads to the left fourth and fifth intercostal spaces along the mid-axillary line results in a change in the cardiac output measurement.

**Methods:**
This was a prospective, controlled, crossover, paired study of 30 patients where electrodes were placed in the recommended positions and cardiac output (CO1) obtained after two minutes. The second cardiac output (CO2) was then obtained with the electrodes Z3 and Z4/EcG3/neutral repositioned at the left mid-axillary line at the fourth and fifth intercostal spaces. The final step involved switching the Z3 and Z4/EcG3/neutral leads back to the recommended position and the cardiac output (CO3) was measured. Results: the average of the initial and third readings (COave) was compared with the measured CO2 and analyzed. The regression equation was: CO at the proposed site (CO2) = COave at the recommended site + 0.058. The paired samples correlation was 0.995. Within the 95 percent limits of agreement, the bias with CO measured at the proposed site of electrode placement was 0.046 L/min with the limits at -0.24 L/min and 0.34 L/min. The mean difference was 0.86% of the average CO.

**Keywords:**
- Electrode placements
- Impedance
- Non-invasive cardiac output monitoring
- PhysioFlow®
2 APPLICATION STUDIES
2.1 CARDIOLOGY

2016 focused update: clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations.

Authors:
• Guazzi M,
• Arena R,
• Halle M,
• Piepoli MF,
• Myers J,
• Lavie CJ.

Abstract:

Noninvasive Determination of CO
Because peak Vo2 is strongly related to the CO response to exercise, peak Vo2 is often considered a surrogate for CO. In fact, one reason that peak Vo2 is such a strong prognostic marker is that it closely parallels cardiac function with exercise. However, peak Vo2 can be influenced by many other factors (including age, sex, motivation, obesity, deconditioning, and localized muscle fatigue).85 Thus, it has been of interest to study whether the noninvasive determination of CO may enhance the prognostic power of CPX. A number of studies have been useful in assessing the complementary value of CO responses to exercise, along with CPX indexes, for evaluating other hemodynamic responses (eg, exercise EF, stroke work index, and other indexes of contractility) and for assessing submaximal hemodynamic responses to exercise. Studies have demonstrated that noninvasively determined peak CO provides an independent predictor of outcomes that enhances the prognostic utility of peak Vo2.86–90 More recent reports suggest that noninvasively determined peak cardiac index complements indexes of ventilatory inefficiency and peak Vo2 and that combining these markers provides the most powerful stratification of risk.91,92 Although the Fick and thermodilution methods remain the gold standards for the measurement of CO,93 several rebreathing methods that use CPX are available. Bioelectric impedance has also experienced a renewed interest in recent years, and along with a number of validation studies, cardiac hemodynamics with these techniques have been shown to have prognostic value in patients with HF.91,92,94–96.

IMPORTANT NOTE FROM THE MANUFACTURER:
These recommendations highlight the necessity to measure CO independently from VO2 in Heart Failure patients in order to considerably increase the predictive value of a cardiopulmonary exercise test. By far the most important study supporting these recommendations comes from Stanford University (Pr. Jonathan Myers), a research and clinical center using PhysioFlow. It is most likely that any other device would not have yield similar results as they are known for underperforming during exercise.
2. Application studies

2.1 Cardiology

Best Detection of Coronary Artery Disease using a New Generation Impedance Cardiography: Comparison to Exercise Thallium 201 Scintigraphy

Authors:
• JM Dupuis,
• F Prunier,
• W Abi-Khalil,
• Ph Pezard,
• F Bour,
• Ph Geslin,
Department of cardiology, C.H.U. Angers France.

Abstract:
During exercise in patients with ischemia, contractility is impeded before electrical signs or angina appear. Therefore, measurement of contractility impairment could provide a highly sensitive approach to the detection of an ischemia. The protocol was designed to determine if a new, non invasive cardiac output measuring device (Physio Flow®: PF03, Manatec France) whose measurements are based on analysis of instant thoracic impedance (ICG) variations could be helpful to detect ischemia during exercise thallium scintigraphy.

Methods:
The efficiency of ICG in detecting myocardial ischemia was compared to treadmill exercise/redistribution thallium-201 scintigraphy. During exercise, patients had simultaneous measurement of stroke volume with ICG. ICG was considered abnormal if stroke volume at the peak of exercise was lower than another stroke volume measured before, and separated by at least 1 min from peak. Clinical was considered as positive if typical angina occurred and an abnormal ECG if ST-segment horizontal or descending depression > 1 mV lasting for at least 30 seconds. Ischemia was affirmed by a mismatch between exercise/redistribution thallium-201 scintigraphy.

Results:
36 patients (30 men, age 62+/−11 years), 30 with proved CAD were submitted to treadmill exercise/redistribution thallium-201 scintigraphy. Stroke volume profile alteration always occurred earlier in exercise than ECG ST segment depression and angina. The sensitivity (Se), specificity (Sp), positive (PPV) and negative (NPV) predictive values are summarized in the following table.

<table>
<thead>
<tr>
<th></th>
<th>Se</th>
<th>Sp</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>46%</td>
<td>74%</td>
<td>50%</td>
<td>71%</td>
</tr>
<tr>
<td>ECG(+)</td>
<td>31%</td>
<td>65%</td>
<td>33%</td>
<td>63%</td>
</tr>
<tr>
<td>ECG(+) and/or Angina</td>
<td>41%</td>
<td>66%</td>
<td>41%</td>
<td>66%</td>
</tr>
<tr>
<td>ECG(+) and Angina</td>
<td>33%</td>
<td>76%</td>
<td>43%</td>
<td>68%</td>
</tr>
<tr>
<td>ICG(-)</td>
<td>100%</td>
<td>74%</td>
<td>67%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Conclusion:
Use of ICG during exercise allows for the estimation of stroke volume changes over time. These preliminary results show that it is a promising technique compared to ECG or other criteria for the detection of ischemia during exercise test with an excellent NPV.
Detection of Coronary Artery Disease (CAD) during Bicycle Exercise, using New Generation Impedance Cardiography

Heart Journal, June 2000 Volume 83 supplement II

Authors: • J.M. Dupuis, • P Abraham, • J. Bour, • K. Kalife. C.H.U. Angers France.

Abstract: During exercise in patients with CAD, contractility is impeded before electrical signs or angina appear. Therefore, measurement of contractility impairment could provide a highly sensitive approach to the detection of CAD. The protocol was designed to determine if a new, non-invasive cardiac output measuring device (Physio Flow®: PF03, Manatec France) whose measurements are based on analysis of instant thoracic impedance (ICG) variations that does not use average impedance baseline values could be helpful to detect CAD.

Methods: On a 12 months period, subjects suspected of CAD had been submitted to an incremental bicycle exercise test (30 W / 2 min). Those who presented either an interpretable and abnormal ECG: [ECG(+)] ST-segment horizontal or descending depression > 1 mV lasting for at least 30 seconds, or typical angina during the exercise test were submitted to coronaryography (n=29. 18 men/11 women, age = 57+/−10 years. Weight = 80+/−12 Kg. Height = 170+/−9 cm). Coronarography, considered as the gold standard for comparison, were performed and analyzed by independent observers and quoted abnormal for at least 50% stenosis of the coronary arteries: coro(+). During exercise, patients had simultaneous measurement of stroke volume with ICG. ICG was considered abnormal if stroke volume at the peak of exercise was lower than another stroke volume measured before, and separated by at least 1 min from peak.

Results: Number of patients in each group are summarized in the table. Stroke volume profile alteration always occurred earlier in exercise than ECG ST segment depression. The sensitivity, specificity, positive and negative predictive values were respectively: 63, 20, 60, 22% for ECG alone; 68, 20, 62, 25 for angina alone; 84, 10, 64, 25% for ECG or angina; 100, 50, 79, 100% for ICG.

<table>
<thead>
<tr>
<th></th>
<th>coro(+) n=19</th>
<th>coro(-) n=10</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG(+)</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Angina</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>ECG(+) and Angina</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>ECG(+) and/or Angina</td>
<td>16</td>
<td>9</td>
</tr>
<tr>
<td>ICG SV depression</td>
<td>19</td>
<td>5</td>
</tr>
</tbody>
</table>

Conclusion: Use of ICG during exercise allows for the estimation of stroke volume changes over time. As such, these preliminary results show that it is a promising technique for the non-invasive diagnosis of CAD.
**2. Application studies**

**2.1 Cardiology**

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**Changes in Transthoracic Impedance Signal Predict Outcome of 70° Head-up Tilt Test**

*Accepted by Clinical Science October 21st 2002*

**Authors:**

- Elisabeth Bellard¹,
- Jacques-Olivier Fortrat¹,
- Daniel Schang²,
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- Georges Lefthériotis¹

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Georges Lefthériotis
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Fax: 0-33-2-41-35-50-42
E-mail: geleftheriotis@chu-angers.fr

**Abstract:**

We determined if the early changes in central hemodynamics determined by transthoracic impedance induced by head-upright tilt test (70°HUT) could predict syncope. Heart rate, arterial blood pressure and central hemodynamics (pre-ejection period and rapid left ventricular ejection time (T1), slow ejection time (T2) and dZ/dtmax, assessed by the transthoracic impedance technique), were recorded during supine rest and 45 min 70°HUT in 68 patients (40±2 years) with history of unexplained recurrent syncope. Thirty-eight patients (42±3 years) had a symptomatic outcome to 70°HUT (fainters) and 30 (39±2 years) had a negative outcome (non-fainters). Between the 5th and 10th minutes of 70°HUT, T2 increased significantly only in the fainters and a change of T2 >40 ms from baseline predicted a positive outcome with a sensitivity of 68% and a specificity of 70%. During supine rest, fainters exhibited a shorter T2 than non-fainters (183±10 ms vs. 233±14 ms, p<0.01). A T2 <199ms predicted a positive 70°HUT outcome with a sensitivity of 68% and a specificity of 63%. The combination to the changes from rest to 70°HUT of the other hemodynamic variables (heart rate >11 bpm, systolic <2 mmHg, diastolic <7 mmHg and pulse <3 mmHg pressures) increased the specificity to 97% as well as the positive predictive value (93%). Transthoracic impedance could detect differences between fainters and non-fainters in central hemodynamics during supine rest and the initial period of 70°HUT with a consistent sensitivity and specificity when combined with peripheral hemodynamic variables.
Head-upright Tilt Test with Sublingual Nitroglycerin Predicts Hemodynamic Abnormalities in 70° Head upright Tilt


Authors:
• Bellard Elisabeth,
• Fortrat Jacques-Olivier,
• Dupuis Jean-Marc,
• Victor Jacques,
• Lefthériotis Georges


Abstract:
We aimed to determine if the outcome to a head upright tilt test (70°HUT) with sublingual nitroglycerin (NTG) could retrospectively help to determine abnormal changes in central and peripheral hemodynamics to a standard (STD) 45 min 70°HUT without NTG in patients with unexplained syncope. 32 patients with negative outcome to a 70°HUT-STD were submitted to consecutive 70°HUT+NTG. Heart rate, arterial blood pressure (BP) and central hemodynamic assessed by transthoracic impedance variables (pre ejection +rapid left ventricular ejection time (T1, ms) and peak of first derivative of signal (dZ/dtmax) were recorded during supine rest, initial 5 min and 40-45 min of a 70°HUT-STD. Changes from rest value of these variables (mean+/-SEM) were retrospectively compared (unpaired T test) between patients with a negative (n=15,NTG-) and positive (n=17,NTG+) outcome to a 70°HUT+NTG. Differences were only observed during 40-45 min of 70°HUT-STD: systolic (NTG+:18+/-4 vs NTG-:-2+/-4 mmHg;p<0.01), mean BP (-1+/-2 vs 6+/-2 mmHg;p<0.05) and dZ/dtmax (-51+/-30 vs 35+/-21 Ohm.s-1;p<0.05). A drop of systolic BP >10mmHg and/or dZ/dtmax >13 Ohm.s-1 predicted positive outcome to 70°HUT+NTG with a sensitivity of 82% and a specificity of 60% suggesting that abnormal response to a 70°HUT+NTG was linked to 70°HUT-STD outcome.
Impedance Cardiography and Quantitative Tissue Doppler Echocardiography for Evaluating the Effect of Cardiac Resynchronization Therapy


**Authors:**
- Hitoshi Adachi, MD; Tomoya Hiratsuji, MD; Shigeki Sakurai, MD; Hiroshi Tada, MD; Takuji Tomoya, Koichi MD FJCC; Shigeto Naito, MD; Hiroshi Hoshizaki, MD; Shigeru Oshima, MD FJCC; Taniguchi, MD FJCC.

**Abstract:**
An 83-year-old woman presented with dilated cardiomyopathy. Cardiac resynchronization therapy was performed. Two weeks later, cardiac output and ventricular wall motion were estimated using impedance cardiography and tissue Doppler echocardiography with and without pacing. Cardiac output increased from 3.5 to 4.5 l/m during biventricular pacing with a 120 msec atrioventricular interval. Intraventricular phase difference for contraction decreased from 190 to 150 msec. When the atrioventricular interval was 180 msec, cardiac output and phase difference became 4.6 l/m and 170 msec. These assessments were performed rapidly and non-invasively. New impedance cardiography and tissue Doppler echocardiography are useful to evaluate the effect of cardiac resynchronization therapy.

**Conclusion:**
The present case demonstrates usefulness of impedance cardiography and tissue Doppler echocardiography in the evaluation of the effect of cardiac resynchronization therapy on cardiac function. Using impedance cardiography, the cardiac output could be assessed easily and non-invasively. Impedance cardiography and tissue Doppler are useful for evaluating the beneficial effect of cardiac resynchronization therapy and determined the optimal AV delay interval.

**References:**
Impedance Cardiography a Rapid and Cost effective Screening Tool for Cardiac Disease

European Journal of Heart Failure, October 2005 (Vol. 7, Issue 6, Pages 974-983)

Authors:
• Jean Bour, MD,
• John Gale Kellett, MD

Abstract:
Impedance cardiography (ICG) charts the rises and falls of thoracic impedance as the fluid content of the chest changes with each heartbeat. Breathing, arrhythmia, movements and posture interfere with the ICG. Modern pattern recognition software can now produce a composite Signal Averaged ICG, which considerably simplifies interpretation.

The first derivative velocity waveform shows a smooth S wave that corresponds with systole, while the second derivative acceleration waveform (dZ/dt) contains several reference points that outline the A-wave, S and O-wave. Normally the A-wave follows atrial contraction and occurs in late diastole. It can, therefore, be abnormal in both atrial and ventricular arrhythmias, and is abnormally increased when there is diastolic dysfunction. The S-wave reflects ventricular contractility, and is deformed by ventricular dyssynchrony. The O-wave is associated with mitral valve opening and is abnormally enlarged in heart failure.

These different patterns of ICG waveform are relatively easy to recognise and can be cost-effectively and quickly obtained to reliably distinguish between normal and abnormal cardiac function.

Keywords:
• Impedance
• Cardiography
• Heart failure
• Diastolic dysfunction
• Dyssynchrony
Isolated Left Ventricular Diastolic Dysfunction: Implications for Exercise Left Ventricular Performance in Patients without Congestive Heart Failure

Journal of the American Society of Echocardiography, Volume 19, Issue 5, Pages 491 - 498

Authors:
• V. Palmieri
• C. Russo
• E. Palmieri
• E. Arezzi
• S. Pezzullo

• S. Minichielo
• S. Martino
• P. Migliaresi
• A. Celentano

Abstract-Objective:
Clinical relevance of left ventricular (LV) diastolic dysfunction in the absence of congestive heart failure (CHF) and LV systolic dysfunction is not fully established.

Methods:
Asymptomatic outpatients, sedentary, with cardiovascular risk factors but no history of cardiovascular events, underwent echocardiographic evaluation of LV structure and function by standard Doppler, color M-mode, and Doppler tissue methods, and exercise testing with simultaneous noninvasive assessment of LV stroke index and cardiac index. LV ejection fraction less than 50% and significant valvular disease or stress test suggestive of coronary disease were additional exclusion criteria.

Results:
In 70 patients selected (40 ± 10 years old, 63% men, 34% hypertensive, 34% diabetic, 4% diabetic and hypertensive, 11% with LV hypertrophy), LV diastolic dysfunction was detected in 26%, which was associated with hypertension, higher LV mass index, lower systolic function, lower peak exercise heart rate, and chronotropic reserve (all P < .05), and with lower peak exercise stroke index and cardiac index (both covariates adjusted P < .05), but not with lower peak exercise metabolic equivalents (P > .5). Abnormal LV relaxation was independently correlated with lower peak exercise cardiac index and stroke index (both P < .05). Peak exercise systolic and cardiac indices were comparable between patients with CHF risk factors (74%) versus those without.

Conclusion:
Isolated LV diastolic dysfunction was independently associated with lower peak exercise LV systolic performance in patients without CHF. Its diagnosis may provide a target for aggressive CHF risk management.
## 2. Application studies

### 2.1 Cardiology

#### Thoracic Bioimpedance for Optimizing Atrioventricular and Intraventricular Delays after Cardiac Resynchronization Therapy

**Authors:**
- Fabrice Bauer, MD, Mathieu Lemercier, MD, Sidney Tapiero, MD, Arnaud Savouré, MD, Bénédicte Godin, MD, Frédéric Anselme, MD, PhD, Alain Cribier, MD, PhD.

**From the Section of Echocardiography, Department of Cardiology, Rouen University Hospital, Rouen, FR. and from unité INSERM U644, Rouen University Medical School, Rouen FR.**

**Abstract-Background:**
The lack of easy and fast method for optimizing AV and VV delay after cardiac resynchronization therapy (CRT), is a major deficiency of two-dimensional echocardiography combined with tissue Doppler imaging (TDI). The aim of our human study was to test a new non-invasive system for optimizing cardiac resynchronization.

**Methods-Results**
Six to 12 months before bioimpedance and 2D echocardiographic study, 10 patients with symptomatic systolic heart failure were resynchronized with CRT device. At the subsequent session, a total of 78 different steady-state hemodynamic conditions were studied by serially changing the pacemaker delays. 2D echocardiography with TDI capability was used as gold standard for optimal cardiac resynchronization.

A validated system was employed for measuring the thoracic electrical bioimpedance (TEB). Physioflow TEB signals were recorded on a computer and left ventricular stroke volume was determined online by morphological analysis of the impedance waveforms. Optimal AV and VV delays by Physioflow TEB were defined when stoke volume was maximal. Optimal VV and AV delays obtained by echocardiography averaged 0±10 ms and 129±18 ms. Those obtained by bioimpedance averaged 0±21 ms and 133±28 ms, respectively. Bland-Altman analysis showed a good agreement between the echocardiography-obtained optimal delays and bioimpedance (mean difference, 2±22ms).

**Conclusion:**
The Physioflow thoracic electrical bioimpedance system provided an accurate approach for adjusting AV and VV delays, suggesting an important application in cardiac resynchronization therapy.

**Keywords:**
- Bioimpedance
- Echocardiography
- Systolic dysfunction
- Heart failure
- Resynchronization therapy
2. Application studies

2.1 Cardiology

Evaluation of a New Noninvasive, Thoracic Bioimpedance Monitor for Hemodynamic Monitoring in Pediatric Patients

Gary R Haynes, PhD, MD and Jeremy Ringwald, MD
Departments of Anesthesia and Perioperative Medicine and Pediatrics, Division of Pediatric Cardiology
Medical University of South Carolina, Charleston, South Carolina

Introduction

Hemodynamic monitoring with a pulmonary artery catheter is a common practice in adults, but anesthesiologists and surgeons rarely use invasive monitoring routinely in pediatric patients because of the technical difficulties and associated risks. A reliable, non-invasive method for determining cardiac output and hemodynamic values may be useful in pediatric patients for optimal management. We report preliminary data evaluating a new thoracic bioimpedance (TBI) system for determination of hemodynamic values in pediatric patients in a prospective, observational study.

Methods

Following Institutional Board Review approval and parental informed consent, we studied 30 patients presented for diagnostic cardiac catheterization. Enrollment was not restricted. All procedures were performed under general anesthesia or moderate sedation. Patients had cardiac output measured by either a modified Fick principle application where oxygen content of arterial and pulmonary artery blood was measured directly and oxygen uptake was estimated or by TBI. Cardiac output determinations of cardiac output were made with the PhysioFlow PFD-7 (Mansatone, Inc., Paris, FR). Cardiac index determinations (Fick or TBI versus CO) were analyzed using the Bland–Altman analysis.

Results

<table>
<thead>
<tr>
<th>Enrollment</th>
<th>N = 38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (year)</td>
<td>2.0 ± 2.5</td>
</tr>
<tr>
<td>Mean MS</td>
<td>24.6</td>
</tr>
<tr>
<td>Mean Weight (Kg)</td>
<td>44.6</td>
</tr>
<tr>
<td>Mean BSA (M2)</td>
<td>0.97 ± 0.29</td>
</tr>
<tr>
<td>Mean BMI (Kg/M2)</td>
<td>19.9 ± 3.6</td>
</tr>
<tr>
<td>Males</td>
<td>20</td>
</tr>
<tr>
<td>Females</td>
<td>18</td>
</tr>
</tbody>
</table>

Cardiac structure
Normal: 21
Anomaly: 22

Cardiac parapathophysiology

Completed studies: PCL-Fick (21)
Incomplete studies: PCL-TDI (22)

TBI determinations of cardiac output were made with the PhysioFlow PFD-7, and a modified Fick method was used to estimate CO in adults. TBI determines CO by measuring the change in an electrical impedance signal. This is measured by attaching skin electrodes at the base of the neck and sternum. Some devices use the absolute values of the signal (Z0), which has been described as a limiting factor in the usefulness of TBI. We evaluated a new monitor that uses relative values of the impedance signal rather than absolute values. This system has good agreement with the TD method for measuring CO in adults.

The data provided by this monitor has good agreement with values obtained by thermodilution. Differences in obtaining simultaneous TBI readings while obtaining blood samples for the modified Fick and using estimates for oxygen uptake instead of measuring oxygen consumption accounts for the greater difference between TBI and Fick CO values. TBI may be a useful method for the noninvasive monitoring of pediatric hemodynamics.

References

New Non Invasive Marker of Heart Failure with Pulmonary Congestion: Thoracic Electrical Bioimpedance

Heart Failure Congress, Milan 2008

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²: C.H.U. Charles Nicolle, Rouen, France

Abstract-Objective:
Brain Natriuretic Peptide (BNP) is usually utilized to diagnose heart failure. However, BNP is expensive, measured invasively and is not specific to the left ventricle. The aim of this study was to calculate the thoracic fluid index (TFI, ohm), a new marker of pulmonary congestion measured using the electrical bioimpedance, and to correlate it to BNP level in normals and patients with heart failure.

Methods-Results:
6 normals and 15 patients with EF < 35% were investigated. The BNP level was measured with the Triage assay (Biosite). A commercially available system for measuring the thoracic bioimpedance (Physioflow, FR) was used for calculating TFI from 4 electrodes (2 at the upper chest and 2 in front of the xyphoid process) connected to a computer interfacing with a dedicated platform. Both BNP level and TFI were measured simultaneously. Mean BNP concentration and TFI were 777 ± 700 pg/ml (range from 5 to 2038 pg/ml) and 114 ± 37 ohm (range from 45 to 170 ohm), respectively. Multiple regression analyses showed a good correlation and agreement between the BNP and TFI (r=0.93, figure. Cut-offs are in represented by dashed lines). Measurement of TFI was obtained in less than 2 minutes.

Conclusion:
The Thoracic Fluid Index provided good estimation of heart failure, suggesting an important application of this new parameter and bioimpedance method to detect heart failure.
Patients with Systolic Heart Failure Show Improvement with Long-Acting, Cardioselective Beta-Blocker Nebivolol when Others Fail

ESC Congress 2007

Authors:
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• M. Lemercier¹,

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Abstract-Purpose:
β-blockers are highly effective by reducing morbimortality in patients with systolic heart failure (SHF). However, failure to (re-)start or to titrate β-blockers is frequent, occurring in 10% of these patients. We hypothesized that β-blockers intolerance is attributable to persistent elevated afterload and that nebivolol would efficiently normalize it.

Patients-METHODS:
We selected 20 SHF patients intolerant to β-blockers. Reasons for intolerance were worsening heart failure and symptomatic peripheral hypoperfusion during up-titration. Using commercially available bioimpedancemeter (Physioflow, FR), we measured cardiac index (CI), total intrathoracic fluid (TIF), blood pressure, heart rate and NYHA functional class with the first β-blocker and after substituting it to equidose nebivolol. Systemic vascular resistance index (SVRi) was calculated along with left cardiac work index (LCWi) using validated equations.

Results-Discussion:
Patients aged 63±15y. Both mean arterial pressure and heart rate significantly decreased with nebivolol from 106±12 to 99±7 mm Hg (p=0.002) and 74±14 to 71±12 (p=0.05), respectively. Effects of replacing the β-blocker to nebivolol are shown in the table. There was a significant improvement in NYHA functional class from 2.9±0.5 to 2.1±0.9 (p=0.001)

CONCLUSION: Patients with systolic heart failure, intolerant to β-blockers, exhibit persistent elevated systemic vascular resistance. By reducing the systemic vascular resistances, nebivolol enhances cardiac output, decreases intrathoracic fluid, and therefore improves NYHA functional class.

<table>
<thead>
<tr>
<th>Hemodynamic Data by Bioimpedance</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI (l/min/m²)</td>
</tr>
<tr>
<td>With the first β-blocker</td>
</tr>
<tr>
<td>Under nebivolol</td>
</tr>
<tr>
<td>SVRi (Dynesxs/cm5/m²)</td>
</tr>
<tr>
<td>LCWi (Jules)</td>
</tr>
<tr>
<td>TIF (1/ohm)</td>
</tr>
</tbody>
</table>

CI: Cardiac Index TIF: Total Intrathoracic Fluid SVRi: Systemic Vascular Resistance index LCWi: Left Cardiac Work index

Conclusion:
Patients with systolic heart failure, intolerant to β-blockers, exhibit persistent elevated systemic vascular resistance. By reducing the systemic vascular resistances, nebivolol enhances cardiac output, decreases intrathoracic fluid, and therefore improves NYHA functional class.
Central hemodynamic responses during high-intensity interval exercise and moderate continuous exercise in patients with chronic heart failure

Citation: The European Journal of Cardiovascular Prevention and Rehabilitation (April 2011) 18 (Supplement 1), S90

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**Topic(s):** Heart Failure (Rehabilitation & Implementation)

**Purpose:**

We have previously proposed an optimized high-intensity interval exercise (HIIE) protocol in patients with chronic heart failure (CHF). However, central hemodynamic response during HIIE has not been studied in patients with CHF. The aim of this study was to compare central hemodynamic responses during our optimized HIIE protocol compared to that of an isocaloric moderate-intensity interval exercise (MICE) session.

**Methods:**

Thirteen CHF patients (59±6 years, NYHA I-III, LVEF 27 %) performed in random order a single session of HIIE (2×8min) consisting in 30s at 100% of maximal aerobic power (MAP) alternating with 30s of passive recovery or an isocaloric MICE (22min) at 60% of MAP. Gas exchange, central hemodynamic measured by cardiac bioimpedance, ECG and blood pressure were monitored continuously. Mean pulmonary VO₂ uptake, cardiac output and arterio-venous differences as well as kinetics of those variables were compared during MICE and HIIE.

**Results:**

See Table 1. A mode effect was noted for pulmonary VO₂ and C(a-v)O₂ kinetics (p<0.0001) with lower values measured during HIIE compared to MICE. A mode effect was noted for cardiac output kinetics (p<0.01) with higher values measured during HIIE vs. MICE.

**Conclusion:**

Compared to MICE, optimized HIIE elicited a greater central hemodynamic response in patients with CHF associated with a lower pulmonary VO₂ uptake and arterio-venous difference. HIIE may be an interesting complementary exercise training modality that could favorably improve central hemodynamic responses during exercise training intervention in patients with CHF.

**Central hemodynamic responses during MICE and HIIE:**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MICE</th>
<th>HIIE</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO₂ (ml/min)</td>
<td>1052±300</td>
<td>977±276</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>9.25±2.33</td>
<td>9.89±4.29</td>
<td>0.0007</td>
</tr>
<tr>
<td>C(a-v)O₂ (ml/100 ml)</td>
<td>11.57±3.42</td>
<td>10.55±3.42</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean power (Watts)</td>
<td>58±17</td>
<td>48±14</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total exercise time</td>
<td>22</td>
<td>8</td>
<td>---</td>
</tr>
</tbody>
</table>
Microvascular oxygen delivery-to-utilization mismatch at the onset of heavy-intensity exercise in optimally treated patients with CHF.


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Abstract:
Impaired muscle blood flow at the onset of heavy-intensity exercise may transiently reduce microvascular O(2) pressure and decrease the rate of O(2) transfer from capillary to mitochondria in chronic heart failure (CHF). However, advances in the pharmacological treatment of CHF (e.g., angiotensin-converting enzyme inhibitors and third-generation beta-blockers) may have improved microvascular O(2) delivery to an extent that intramyocyte metabolic inertia might become the main locus of limitation of O(2) uptake (Vo(2)) kinetics. We assessed the rate of change of pulmonary Vo(2) (Vo(2)(p)), (estimated) fractional O(2) extraction in the vastus lateralis (approximately Delta[deoxy-Hb+Mb] by near-infrared spectroscopy), and cardiac output (Qt) during high-intensity exercise performed to the limit of tolerance (Tlim) in 10 optimally treated sedentary patients (ejection fraction = 29 + or - 8%) and 11 controls. Sluggish Vo(2)(p) and Qt kinetics in patients were significantly related to lower Tlim values (P < 0.05). The dynamics of Delta[deoxy-Hb+Mb], however, were faster in patients than controls [mean response time (MRT) = 15.9 + or - 2.0 s vs. 19.0 + or - 2.9 s; P < 0.05] with a subsequent response "overshoot" being found only in patients (7/10). Moreover, tauVo(2)/MRT-[deoxy-Hb+Mb] ratio was greater in patients (4.69 + or - 1.42 s vs. 2.25 + or - 0.77 s; P < 0.05) and related to Qt kinetics and Tlim (R = 0.89 and -0.78, respectively; P < 0.01). We conclude that despite the advances in the pharmacological treatment of CHF, disturbances in "central" and "peripheral" circulatory adjustments still play a prominent role in limiting Vo(2)(p) kinetics and tolerance to heavy-intensity exercise in nontrained patients.
Cardiopulmonary and Noninvasive Hemodynamic Responses to Exercise Predict Outcomes in Heart Failure

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Abstract-Background:
An impaired cardiac output response to exercise is a hallmark of chronic heart failure (HF). We determined the extent to which noninvasive estimates of cardiac hemodynamics during exercise in combination with cardiopulmonary exercise test (CPX) responses improved the estimation of risk for adverse events in patients with HF.

Keywords:
• Exercise testing
• Oxygen uptake
• Cardiac Output
• Mortality

Methods-Results:
CPX and impedance cardiography were performed in 639 consecutive patients (mean age 48 ± 14 years), evaluated for HF. Clinical, hemodynamic, and CPX variables were acquired at baseline and subjects were followed for a mean of 460 ± 332 days. Patients were followed for the composite outcome of cardiac-related death, hospitalization for worsening HF, cardiac transplantation, and left ventricular assist device implantation. Cox proportional hazards analyses including clinical, noninvasive hemodynamic, and CPX variables were performed to determine their association with the composite endpoint. There were 113 events. Among CPX variables, peak oxygen uptake (VO2) and the minute ventilation (VE)/carbon dioxide production (VCO2) slope were significant predictors of risk for adverse events (age-adjusted hazard ratio [HR] 1.08, 95% confidence interval [CI] 1.05–1.11 for both; P < .001). Among hemodynamic variables, peak cardiac index was the strongest predictor of risk (HR 1.08, 95% CI 1.0–1.16; P = .01). In a multivariate analysis including CPX and noninvasively determined hemodynamic variables, the most powerful predictive model included the combination of peak VO2, peak cardiac index, and the VE/VCO2 slope, with each contributing significantly and independently to predicting risk; an abnormal response for all 3 yielded an HR of 5.1 (P < .001).

Conclusion:
These findings suggest that noninvasive indices of cardiac hemodynamics complement established CPX measures in quantifying risk in patients with HF.
Cardiopulmonary Responses and Prognosis in Hypertrophic Cardiomyopathy: A Potential Role for Comprehensive Noninvasive Hemodynamic Assessment.

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5 Veterans Affairs Palo Alto Health Care System, Palo Alto, California. Stanford Cardiovascular Institute and Biotronik Italia funded the research. Dr. Magavern is funded by the Sarnoff Cardiovascular Research Foundations. Dr. Ashley is the co-founder of and owns stock options in Personalis, Inc. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Objectives:
The study sought to discover the key determinants of exercise capacity, maximal oxygen consumption (oxygen uptake [VO2]), and ventilatory efficiency (ventilation/carbon dioxide output [VE/VCO2] slope) and assess the prognostic potential of metabolic exercise testing in hypertrophic cardiomyopathy (HCM).

Methods:
The study sample included 156 HCM patients consecutively enrolled from 2007 to 2012 with a complete clinical assessment, including rest and stress echocardiography and cardiopulmonary exercise test (CPET) with impedance cardiography. Patients were also followed for the composite outcome of cardiac-related death, heart transplant, and functional deterioration leading to septal reduction therapy (myectomy or septal alcohol ablation).

Results:
Abnormalities in CPET responses were frequent, with 39% (n = 61) of the sample showing a reduced exercise tolerance (VO2 max <80% of predicted) and 19% (n = 30) characterized by impaired ventilatory efficiency (VE/VCO2 slope >34). The variables most strongly associated with exercise capacity (expressed in metabolic equivalents), were peak cardiac index (r = 0.51, p < 0.001), age (r = 0.25, p < 0.01), male sex (r = 0.24, p = 0.02), and indexed right ventricular end-diastolic area (r = 0.31, p = 0.002), resulting in an R2 of 0.51, p < 0.001. Peak cardiac index was the main predictor of peak VO2 (r = 0.61, p < 0.001). The variables most strongly related to VE/VCO2 slope were E/E0 (r = 0.23, p = 0.021) and indexed left atrial volume (LAVI) (r = 0.34, p = 0.005) (model R2 = 0.15). The composite endpoint occurred in 21 (13%) patients. In an exploratory analysis, 3 variables were independently associated with the composite outcome (mean follow-up 27 _ 11 months): peak VO2 <80% of predicted (hazard ratio: 4.11; 95% confidence interval [CI]: 1.46 to 11.59; p = 0.008), VE/VCO2 slope >34 (hazard ratio: 3.14; 95% CI: 1.26 to 7.87; p = 0.014), and LAVI >40 ml/m2 (hazard ratio: 3.32; 95% CI: 1.08 to 10.16; p = 0.036).

Conclusion:
In HCM, peak cardiac index is the main determinant of exercise capacity, but it is not significantly related to ventilatory efficiency. Peak VO2, ventilatory inefficiency, and LAVI are associated with an increased risk of major events in the short-term follow-up. (J Am Coll Cardiol HF 2015;--:-- --) © 2015 by the American College of Cardiology Foundation.
Exercise Cardiac Output Limitation in Pectus Excavatum

J Am Coll Cardiol. 2015;66(8):976-977. doi:10.1016/j.jacc.2015.06.1087

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• Géraud Galvaing, MD;
• Fabrice Kwiatkowski, MSc;
• Frédéric Costes, MD, PhD;
• Ruddy Richard, MD, PhD

Abstract:
Indication of pectus excavatum (PE) surgical treatment is a much-debated subject, especially regarding functional impact of the deformation. The pulmonary consequences of PE have been found not to be the limiting factor in exercise for these patients. On the other hand, the hemodynamic consequences of PE have been sparingly studied, because of the difficulty to secure reliable exercise cardiac output (CO). Opinions, therefore, differ greatly as to the scope and the reversibility of hemodynamic exercise limitations for these patients (1,2).

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Usefulness of stroke volume monitoring during upright ramp incremental cycle exercise in young patients with Fontan circulation

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Abstract:
Background: Aerobic capacity (VO2 max) of patients with Fontan circulation (FC) is lowest within patients with congenital heart disease. The reasons have not been completely elucidated.

Methods: Twenty five young patients with non-failing FC underwent a cardiopulmonary test during an upright ramp cycling. By using a signal morphology impedance cardiography device (physioflow®), stroke volume (SV) was evaluated along with effort. The results were compared with paired healthy controls.

Results: FC patients had lower VO2max (24 vs 32ml/Kg/min) and maximal cardiac index (CI) (6.4 vs 9.9 l/min/m²) than controls, due to impaired maximal SV (42 vs 54 ml/m²) and maximal Heart Rate (HR) (154 vs 184/min) (p < 0.001). No correlation between SV and HR at peak was found. At ventilatory threshold, SV continued to rise in a part of FC patients. Other FC patients showed an almost a “plateau” as in controls. The more maximal CI was impaired, the more was maximal arterio-venous difference (r=−0.6, p=0.001). Compared to controls, stroke work was lower in FC patients (p < 0.01) even though maximal vascular resistance was higher in them (p < 0.001).

Conclusion:
Impaired SV and chronotropic incompetence are both independently responsible for impaired CI at peak. The increase in arteriovenous difference appeared to be an adaptive response. As the stroke work was low among FC patients, high systemic vascular resistance does not appear to be the cause of SV impairment but rather a consequence. SV monitoring at effort evidences heterogeneous SV profiles among FC patients that could be considered for the management of patients.
Cardiac output response to exercise in chronic cardiac failure patients.


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**Abstract:**

The purpose of this study was to investigate the precise pattern of stroke volume (SV) response during exercise in patients with chronic heart failure (CHF) compared with age-matched controls. Fourteen patients with CHF and 7 controls performed symptom-limited bicycle exercise testing with respiratory gas exchange measurement. Patients were classified into group A (n = 7) with peak VO2 ≥ 18.0 mL/kg/minute and group B (n = 7) with peak VO2 < 18.0 mL/kg/minute. SV and cardiac output (CO) were continuously measured during exercise using a novel thoracic impedance method (Physioflow). CO and SV were lower in the group B patients than those in controls at peak exercise [CO: 11.3 ± 1.0 (SE) versus 15.6 ± 0.9 L/minute, P < 0.05, SV: 89 ± 6 versus 110 ± 6 mL, P < 0.05]. SV reached its peak levels during submaximal exercise and remained close to the peak value until peak exercise in 6 of 7 group B patients (86%). On the other hand, it progressively increased until peak exercise in 6 of 7 controls (86%) and 5 of 7 group A patients (71%). In all subjects, CO at peak exercise was more closely correlated with SV at peak exercise (r = 0.86, P < 0.001) than with peak heart rate (r = 0.69, P < 0.001). CHF patients with impaired exercise capacity had attenuated increment of CO during exercise, and SV reached its peak levels during submaximal exercise.
Reliability of peak exercise stroke volume assessment by impedance cardiography in patients with residual right outflow tract lesions after congenital heart disease repair

Abstract:
Global ventricular response to exercise may be useful in follow-up of patients with residual right outflow tract lesions after congenital heart disease repair. In this context, impedance cardiography is considered accurate for stroke volume (SV) measurement during exercise testing, however, to date, only partial assessment of its reliability has been reported. We retrospectively evaluated relative and absolute reliability of peak SV by impedance cardiography during exercise using intraclass correlation (ICC) and standard error of measurement (SEM) in this population. Peak SV was measured in 30 young patients (mean age 14.4 years ± 2.1) with right ventricular outflow tract reconstruction who underwent two cardiopulmonary exercise tests at a mean one-year interval. SV was measured using a signal morphology impedance cardiography analysis device (PhysioFlow®) and was indexed to body surface area. ICC of peak indexed SV measurement was 0.80 and SEM was 10.5%. High heterogeneity was seen when comparing patients according to peak indexed SV; in patients with peak SV < 50 ml/m (15 patients), ICC rose to 0.95 and SEM dropped to 2.7%, while in patients with a peak SV > 50 ml/m relative and absolute reliability decreased (ICC = 0.45, SEM = 12.2%). Peak exercise SV assessment by a PhysioFlow device represents a highly reliable method in patients with residual right outflow tract lesions after congenital heart disease repair, especially in patients with peak SV < 50 ml/m. In this latter group, a peak SV decrease > 7.3% (corresponding to the minimum “true” difference) should be considered a clinically-relevant decrease in global ventricular performance and taken into account when deciding whether to perform residual lesion removal.

Keywords:
- Congenital heart disease
- Reliability
- Cardiopulmonary exercise test
- Stroke volume
- Signal morphology impedance cardiography

DOI (Digital Object Identifier) https://doi.org/10.1007/s00246-017-1725-3
Vasoconstrictive Response in the Vascular Beds of the Non-Exercising Forearm during Leg Exercise in Patients with Mild Chronic Heart Failure

Received July 25, 2006; revised manuscript received February 15, 2007; accepted March 2, 2007

Authors:
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Abstract:
Background reduced exercise capacity may be related to decreased redistribution of blood flow from the non-exercising tissues to the exercising skeletal muscle in patients with mild chronic heart failure (CHF). Methods and Results In the present study 14 patients with mild CHF and 10 healthy subjects (N) underwent symptom-limited multistage-ergometer exercise, during which forearm vascular resistance (FVR), cardiac index (CI), systemic vascular resistance index (SVRI), and oxygen uptake (VO₂) were measured non-invasively using the plethysmograph, impedance, and respiratory gas analysis methods, respectively. The VO₂ and CI at peak exercise were lower (p<0.01 each), and SVRI and FVR at both rest and peak exercise were higher in the CHF group than in N. However, both the percent increase in FVR and percent decrease in SVRI from the resting state to peak exercise were lower in CHF than N, and both of them correlated with not only peak VO₂, but also the corresponding resting value of FVR and SVRI (p<0.01 each). Conclusions Redistribution of blood flow from the non-exercising tissues to the working skeletal muscles, which may participate in exercise capacity, can be blunted in CHF. The decreased vasoconstrictive response in the non-exercising tissues is intimately related to the increased resting vascular tone in CHF.

Conclusion:
Not only an impaired reduction in SVRI, mainly because of attenuated reduction of working vascular resistance, but also blunted redistribution of blood flow from non-working to exercising muscles, which is expected from the attenuation of the % increase in FVR, may play a role in the exercise intolerance of CHF patients. The development of a new strategy for alleviating these abnormalities in the nonexercising vascular bed, as well as the impaired vascular relaxation in exercising skeletal muscle, is recommended to ameliorate the decreased exercise capacity of CHF patients.
Haemodynamics during Exercise are a Better Measure of Vasodilator Response in Human Subjects with Pulmonary Hypertension

Accepted for the British Thoracic Society winter meeting

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Abstract:
Patients with pulmonary hypertension (PHT) are deemed ‘non-responders’ (NR) if they show no response to vasodilators at rest. We therefore decided to investigate the effects of vasodilators on pulmonary haemodynamics during exercise.

Methods:
We investigated 4 patients, (2 female, 2 male) with PHT to determine pressure and flow changes over a range of flows. Flow was changed by straight leg raising. A micromanometer tipped continuous pulmonary artery pressure (PAP) catheter was inserted. All 4 were non-responders to a vasodilator challenge (defined as a reduction of >20% in pulmonary vascular resistance). Resting pressure was measured and then 3 mins of supine alternate straight leg raising was performed, whilst the subjects inhaled air or nitric oxide (NO, 40-80 ppm) and oxygen (O2, 15L min). Cardiac Output (CO) was measured by non-invasive impedance cardiography. Subject data was pooled using the method described by Poon (J. Appl Physiol. 1998; 64:854-9). The best-fit line for Pressure Flow (P-Q) plots was determined by linear regression. An adjusted two paired student t-test was used to compare the line gradients.

Results
We found that although total pulmonary vascular resistance (as defined as mean PAP/CO) showed no change at rest, the slope of the P-Q plots decreased with vasodilators during exercise (p<0.0005).

Conclusion:
In each of these 4 subjects, whilst there was no vasodilator response at rest, there was an improving relationship between pressure and flow during exercise whilst receiving the vasodilators NO & O2. In patients with PHT, the assessment of vasodilator response may be better performed during exercise than at rest.
Dynamic Monitoring during Exercise in Familial Amyloid Polyneuropathy (FAP) Type I

Respiration and Circulation (Japan), vol. 51 No.12, December 2003

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Abstract:
A 64-years-old man was admitted to our hospital with complaints of orthostatic faintness and occasional diarrhea. An echocardiogram of the left ventricle demonstrated a severe restrictive disorder and granular sparkling appearance in the thickened walls. Microscopic findings of the myocardial biopsy revealed massive intramuscular accumulation of eosinophilic exudates and severe atrophy of myocytes. Cardiac 99m Tc-pyrophosphate (PYP) findings showed diffuse marked uptake in both left and right ventricles. Cardiac 123I-meta-iodobenzyl-guanidine (MIBG) findings showed complete defect on both early and delayed images. Genetic analysis revealed a single amino acid substitution at codon 30 of transthyretine (TTR), named FAP type I. Dynamic monitoring of the cardiac index peripheral vascular resistance in postural positions and exercise was measured by non-invasive methods (PhysioFlow™ Lab-1). The results of analysis indicated that the fall in blood pressure during exercise in our case was markedly affected by the lowering of peripheral vascular resistance. The cardiac index showed almost the same value during monitoring.

These findings suggest that orthostatic hypotension without increase in heart rate and output in a denervated myocardium is markedly accelerated by peripheral vascular sympathetic denervation in FAP type I. The present case is considered to be the first one encountered in Shiga.

Keywords:
• FAP type I,
• Cardiac amyloidosis,
• PhysioFlow™ Lab-1
Unique cardiac response during apneas in obstructive sleep apnea (OSA) patients

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Introduction:
Negative intrathoracic pressure (NIP) is a defining feature of OSA that acutely augments demand on cardiac function during apneas. Previous studies have shown distinct hemodynamic changes in healthy subjects undergoing simulated apneas. We sought to investigate the cardiovascular effects of NIP during and after a simulated apnea in awake patients with OSA versus healthy subjects.

Methods:
Subjects included 15 healthy males (Mean ± SD: age = 38.6 ± 6.3 yr; BMI = 22.7 ± 5.4; all low risk by Berlin questionnaire; neck circumference = 38.7 ± 2.4) and 10 recently diagnosed OSA patients (age = 44.3 ± 10.7 yr; BMI = 33.3 ± 8.0; AHI = 45.4 ± 37.1). Cardiac function was monitored by non-invasive bioimpedance at baseline and during and 3 minutes after two 30-second Mueller maneuvers (MM).

Results:
During simulated apneas, stroke volume (SV) decreased in both groups with no response difference between control and OSA groups (-5.4 ± 6.5 % and -2.7 ± 11.0 %, p=0.5, respectively). When compared on myocardial contractility index (MCI), the OSA group showed an increase (11.8 ± 14.3 %) and controls a decrease (-7.5 ± 4.9%; p<0.0001) during apnea. In the post-apnea period, SV in controls increased in a compensatory fashion and returned to baseline by the end of the 3 minutes. In contrast, SV declined in OSA patients to pre-apnea values 30 seconds after breathing was restored, suggesting a blunted response. Post-apnea, MCI was different only immediately after termination of the MM, when the OSA response was higher than for controls (18.9 ± 27.5 % versus -8.5 ± 11.9 %, p<0.004).

Conclusion:
NIP appears to provoke unique hemodynamic changes in patients with untreated OSA. This indicates possible chronic adaptations of left ventricle arising from repetitive nocturnal apneas in untreated OSA.

Support: Study supported by NeuMeDx Inc.
**CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

Respiratory muscle unloading improves leg muscle oxygenation during exercise in patients with COPD

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**Background:**

Respiratory muscle unloading during exercise could improve locomotor muscle oxygenation by increasing oxygen delivery (higher cardiac output and/or arterial oxygen content) in patients with chronic obstructive pulmonary disease (COPD).

**Methods:**

Sixteen non-hypoxaemic men (forced expiratory volume in 1 s 42.2 (13.9)% predicted) undertook, on different days, two constant work rate (70–80% peak) exercise tests receiving proportional assisted ventilation (PAV) or sham ventilation. Relative changes (Δ%) in deoxyhaemoglobin (HHb), oxyhaemoglobin (O2Hb), tissue oxygenation index (TOI) and total haemoglobin (Hbtot) in the vastus lateralis muscle were measured by near-infrared spectroscopy. In order to estimate oxygen delivery (DO2est, l/min), cardiac output and oxygen saturation (SpO2) were continuously monitored by impedance cardiography and pulse oximetry, respectively.

**Results:**

Exercise tolerance (Tlim) and oxygen uptake were increased with PAV compared with sham ventilation. In contrast, end-exercise blood lactate/Tlim and leg effort/Tlim ratios were lower with PAV (p<0.05). There were no between-treatment differences in cardiac output and SpO2 either at submaximal exercise or at Tlim (ie, DO2est remained unchanged with PAV; p>0.05). Leg muscle oxygenation, however, was significantly enhanced with PAV as the exercise-related decrease in Δ(O2Hb)% was lessened and TOI was improved; moreover, Δ(Hbtot)% an index of local blood volume, was increased compared with sham ventilation (p<0.01).

**Conclusion:**

Respiratory muscle unloading during high-intensity exercise can improve peripheral muscle oxygenation despite unaltered systemic DO2 in patients with advanced COPD. These findings might indicate that a fraction of the available cardiac output had been redirected from ventilatory to appendicular muscles as a consequence of respiratory muscle unloading.
2. Application studies

2.2 Lung Disease and Internal Medicine

Skeletal muscle reoxygenation after high-intensity exercise in mitochondrial myopathy.


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**Abstract:**
This study addressed whether O(2) delivery during recovery from high-intensity, supra-gas exchange threshold exercise would be matched to O(2) utilization at the microvascular level in patients with mitochondrial myopathy (MM). Off-exercise kinetics of (1) pulmonary O(2) uptake [Formula: see text] (2) an index of fractional O(2) extraction by near-infrared spectroscopy (Δ[deoxy-Hb + Mb]) in the vastus lateralis and (3) cardiac output (Q (T) (') ) by impedance cardiography were assessed in 12 patients with biopsy-proven MM (chronic progressive external ophthalmoplegia) and 12 age- and gender-matched controls. Kinetics of [Formula: see text] were significantly slower in patients than controls (τ = 53.8 ± 16.5 vs. 38.8 ± 7.6 s, respectively; p < 0.05). Q (T) (’) , however, declined at similar rates (τ = 64.7 ± 18.8 vs. 73.0 ± 21.6 s; p > 0.05) being typically slower than [Formula: see text] in both groups. Importantly, Δ[deoxy-Hb + Mb] dynamics (MRT) were equal to, or faster than, [Formula: see text] in patients and controls, respectively. In fact, there were no between-group differences in [Formula: see text]/MRTΔ[deoxy-Hb + Mb] (1.1 ± 0.4 vs. 1.0 ± 0.2, p > 0.05) thereby indicating similar rates of microvascular O(2) delivery. These data indicate that the slower rate of recovery of muscle metabolism after high-intensity exercise is not related to impaired microvascular O(2) delivery in patients with MM. This phenomenon, therefore, seems to reflect the intra-myocyte abnormalities that characterize this patient population.
Haemodynamic effects of proportional assist ventilation during high-intensity exercise in patients with chronic obstructive pulmonary disease.


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Background & Objective:
Proportional assist ventilation (PAV) has been proposed as a more physiological modality of non-invasive ventilation, thereby reducing the potential for deleterious cardio-circulatory effects during exercise, in patients with COPD. We therefore evaluated whether PAV modulates the kinetic and 'steady-state' haemodynamic responses to exercise in patients with moderate-to-severe COPD.

Methods:
Twenty patients underwent constant-load (75-80% peak work rate) cycle ergometer exercise testing to the limit of tolerance (T(lim)), while receiving PAV or breathing spontaneously. Stroke volume (SV), heart rate (HR) and cardiac output (CO) were monitored by impedance cardiography.

Results:
Compared with unassisted breathing, PAV increased T(lim) in 8/20 patients (median improvement 113% (range 8 to 212) vs -20% (range -40 to -9)). PAV had no significant effects on 'steady-state' haemodynamic responses either in patients with or those without increased T(lim) (P > 0.05). However, at the onset of exercise, SV kinetics were slowed with PAV, in 13/15 patients with analysable data. HR dynamics remained unaltered or failed to accelerate sufficiently in nine of these patients, thereby slowing CO kinetics (T(1/2) 61 s (range 81-30) vs 89 s (range 100-47)). These deleterious effects were not, however, associated with PAV-induced changes in T(lim) (P > 0.05).

Conclusion:
PAV slowed the SV and CO kinetics at the onset of high-intensity exercise in selected patients with moderate-to-severe COPD. However, these adverse effects of PAV disappeared during the stable phase of exercise, and were not related to the ergogenic potential of PAV in this patient population.

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Effects of hyperoxia on the dynamics of skeletal muscle oxygenation at the onset of heavy-intensity exercise in patients with COPD.


Authors:
- Siqueira AC,
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Abstract:
This study addressed whether hyperoxia (HiOX=50% O2), compared to normoxia, would improve peripheral muscle oxygenation at the onset of supra-gas exchange threshold exercise in patients with chronic obstructive pulmonary disease (COPD) who were not overtly hypoxemic (resting PaO2 > 60 mmHg). Despite faster cardiac output and improved blood oxygenation, HiOX did not significantly change pulmonary O2 uptake kinetics (VO2p). Surprisingly, however, HiOX was associated with faster fractional O2 extraction (approximately Delta[deoxy-Hb+Mb] by near-infrared spectroscopy) (p<0.05). In addition, an "overshoot" in Delta[deoxy-Hb+Mb] was found after the initial fast response only in HiOX (7/11 patients) thereby suggesting impaired intra-muscular O2 delivery (Q'O2mv)-to-utilization. These data indicate that, despite improved "central" O2 delivery, Q'O2mv adapted at a slower rate than muscle VO2 under HiOX in non-hypoxaemic patients with COPD. Our results question the rationale of using supplemental O2 to improve muscle oxygenation during the transition to high-intensity exercise in this patient sub-population.
Influence of respiratory pressure support on hemodynamics and exercise tolerance in patients with COPD.


Authors:
- Oliveira CC
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Erratum in

Abstract:
Inspiratory pressure support (IPS) plus positive end-expiratory pressure (PEEP) ventilation might potentially interfere with the "central" hemodynamic adjustments to exercise in patients with chronic obstructive pulmonary disease (COPD). Twenty-one non- or mildly-hypoxemic males (FEV₁ = 40.1 +/- 10.7% predicted) were randomly assigned to IPS (16 cmH(2)O) + PEEP (5 cmH(2)O) or spontaneous ventilation during constant-work rate (70-80% peak) exercise tests to the limit of tolerance (T (lim)). Heart rate (HR), stroke volume (SV), and cardiac output (CO) were monitored by transthoracic cardioimpedance (Physioflow, Manatec, France). Oxyhemoglobin saturation was assessed by pulse oximetry (SpO₂). At similar SpO₂, IPS(16) + PEEP(5) was associated with heterogeneous cardiovascular effects compared with the control trial. Therefore, 11 patients (Group A) showed stable or increased Delta "isotime" - rest SV [5 (0-29) mL], lower DeltaHR but similar DeltaCO. On the other hand, DeltaSV [-10 (-15 to -3) mL] and DeltaHR were both lower with IPS(16) + PEEP(5) in Group B (N = 10), thereby reducing DeltaCO (p < 0.05). Group B showed higher resting lung volumes, and T (lim) improved with IPS(16) + PEEP(5) only in Group A [51 (-60 to 486) vs. 115 (-210 to 909) s, respectively; p < 0.05]. We conclude that IPS(16) + PEEP(5) may improve SV and exercise tolerance in selected patients with advanced COPD. Impaired SV and CO responses, associated with a lack of enhancement in exercise capacity, were found in a sub-group of patients who were particularly hyperinflated at rest.
Inspiratory resistive loading after all-out exercise improves subsequent performance.


Authors:

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Abstract:

We have previously shown that post-exercise inspiratory resistive loading (IRL) reduces blood lactate ([Lac(b)(-)]). In this study, we tested the hypothesis that IRL during recovery could improve subsequent exercise performance. Eight healthy men underwent, on different days, two sequential 30-s, cycle ergometer Wingate tests. During the 10-min recovery period from test 1, subjects breathed freely or through an inspiratory resistance (15 cm H(2)O) with passive leg recovery. Arterialized [Lac(b)(-)] values, perceptual scores (Borg), cardiac output by impedance cardiography (QT), and changes in the deoxygenation status of the M. vastus lateralis by near-infrared spectroscopy (DeltaHHb), were recorded. [Lac(b)(-)] was significantly reduced after 4 min of recovery with IRL (peak [Lac(b)(-)] 12.5 +/- 2.3 mmol l(-1) with free-breathing vs. 9.8 +/- 1.5 mmol l(-1) with IRL). Effort perception was reduced during late recovery with IRL compared with free-breathing. Cardiac work was increased with IRL, since heart rate and QT were elevated during late recovery. Peripheral muscle reoxygenation, however, was significantly impaired with IRL, suggesting that post-exercise convective O(2) delivery to the lower limbs was reduced. Importantly, IRL had a dual effect on subsequent performance, i.e., improvement in peak and mean power, but increased fatigue index (P < 0.05). Our data demonstrate that IRL after a Wingate test reduces post-exercise effort perception and improves peak power on subsequent all-out maximal-intensity exercise.
Effects of respiratory muscle unloading on leg muscle oxygenation and blood volume during high-intensity exercise in chronic heart failure.


**Authors:**
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**Abstract:**
Blood flow requirements of the respiratory muscles (RM) increase markedly during exercise in chronic heart failure (CHF). We reasoned that if the RM could subtract a fraction of the limited cardiac output (QT) from the peripheral muscles, RM unloading would improve locomotor muscle perfusion. Nine patients with CHF (left ventricle ejection fraction = 26 +/- 7%) undertook constant-work rate tests (70-80% peak) receiving proportional assisted ventilation (PAV) or sham ventilation. Relative changes (Delta%) in deoxy-hemoglobin, oxy-Hb ([O2Hb]), tissue oxygenation index, and total Hb ([HbTOT], an index of local blood volume) in the vastus lateralis were measured by near infrared spectroscopy. In addition, QT was monitored by impedance cardiography and arterial O2 saturation by pulse oximetry (SpO2). There were significant improvements in exercise tolerance (Tlim) with PAV. Blood lactate, leg effort/Tlim and dyspnea/Tlim were lower with PAV compared with sham ventilation (P < 0.05). There were no significant effects of RM unloading on systemic O2 delivery as QT and SpO2 at submaximal exercise and at Tlim did not differ between PAV and sham ventilation (P > 0.05). Unloaded breathing, however, was related to enhanced leg muscle oxygenation and local blood volume compared with sham, i.e., higher Delta([O2Hb])% and Delta([HbTOT])%, respectively (P < 0.05). We conclude that RM unloading had beneficial effects on the oxygenation status and blood volume of the exercising muscles at similar systemic O2 delivery in patients with advanced CHF. These data suggest that blood flow was redistributed from respiratory to locomotor muscles during unloaded breathing.
Kinetics of muscle deoxygenation are accelerated at the onset of heavy-intensity exercise in patients with COPD: relationship to central cardiovascular dynamics.


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**Abstract:**
Patients with chronic obstructive pulmonary disease (COPD) have slowed pulmonary O(2) uptake (Vo(2)(p)) kinetics during exercise, which may stem from inadequate muscle O(2) delivery. However, it is currently unknown how COPD impacts the dynamic relationship between systemic and microvascular O(2) delivery to uptake during exercise. We tested the hypothesis that, along with slowed Vo(2)(p) kinetics, COPD patients have faster dynamics of muscle deoxygenation, but slower kinetics of cardiac output (Qt) following the onset of heavy-intensity exercise. We measured Vo(2)(p), Qt (impedance cardiography), and muscle deoxygenation (near-infrared spectroscopy) during heavy-intensity exercise performed to the limit of tolerance by 10 patients with moderate-to-severe COPD and 11 age-matched sedentary controls. Variables were analyzed by standard nonlinear regression equations. Time to exercise intolerance was significantly (P < 0.05) lower in patients and related to the kinetics of Vo(2)(p) (r = -0.70; P < 0.05). Compared with controls, COPD patients displayed slower kinetics of Vo(2)(p) (42 +/- 13 vs. 73 +/- 24 s) and Qt (67 +/- 11 vs. 96 +/- 32 s), and faster overall kinetics of muscle deoxy-Hb (19.9 +/- 2.4 vs. 16.5 +/- 3.4 s). Consequently, the time constant ratio of O(2) uptake to mean response time of deoxy-Hb concentration was significantly greater in patients, suggesting a slower kinetics of microvascular O(2) delivery. In conclusion, our data show that patients with moderate-to-severe COPD have impaired central and peripheral cardiovascular adjustments following the onset of heavy-intensity exercise. These cardiocirculatory disturbances negatively impact the dynamic matching of O(2) delivery and utilization and may contribute to the slower Vo(2)(p) kinetics compared with age-matched controls.
2. Application studies
2.2 Lung Disease and Internal Medicine

Evaluation of intradialytic hypotension using impedance cardiography

Int Urol Nephrol. 2010 May 7. [Epub ahead of print]

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Background:
Hypotension during hemodialysis is frequent in patients with cardiovascular disease who have a limited physiological compensatory response. Recent advances in technology allow non-invasive monitoring of cardiac output and derived hemodynamic parameters. This prospective study evaluated episodes of intradialytic hypotension using clinical data and continuous non-invasive hemodynamic monitoring by impedance cardiography.

Methods:
Forty-eight chronic hemodialysis patients, with prevalence for intradialytic hypotensive episodes, underwent evaluation with non-invasive impedance cardiography (Physioflow(R)) before, during and after a regular dialysis session.

Results:
During continuous non-invasive cardiac monitoring, a fall of systolic arterial blood pressure of 20% or more at least once during hemodialysis was detected in 18 patients (37.5%)-thereafter identified as the "Unstable" group. In 30 patients-thereafter called the "Stable" group, the blood pressure did not change significantly. During hypotension, a decrease in cardiac output was found in 11 of the 18 unstable patients, and a significant fall in peripheral resistance in the remaining 7. End-diastolic filling ratio was significantly lower in the unstable group. The most significant predictors associated with intradialytic hypotension were the presence of ischemic heart disease (P = 0.05), and medication with beta blockers (P = 0.037) and calcium channel blockers (P = 0.018).

Conclusion:
Hemodynamic changes in dialysis patients with hypotensive episodes included decreased cardiac output or decreased peripheral resistance. A lower end-diastolic filling ratio may be regarded as a marker for reduced preload in these patients. Non-invasive impedance cardiography may be used to evaluate risk factors for hypotension in dialysis patients.

PMID: 20449654 [PubMed - as supplied by publisher]
Use Of Bioimpedance To Assess Changes In Hemodynamics During Acute Administration Of Continuous Positive Airway Pressure

C44 CARDIOPULMONARY INTERACTIONS AND NON-PULMONARY CRITICAL CARE / Thematic Poster Session / Tuesday, May 18/8:15 AM-4:00 PM / Area H, Hall G (First Level), Morial Convention Center

Authors:
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Rationale:
Attempts to investigate the mechanisms by which continuous positive airway pressure (CPAP) therapy improves heart function in patients with obstructive sleep apnea (OSA) have been limited by the lack of non-invasive methods to assess cardiac performance. Measurements using transthoracic electrical bioimpedance (TEB) correlate closely with cardiac output measurements obtained by pulmonary artery catheterization (PAC). We used TEB to assess acute hemodynamic changes including heart rate (HR), stroke volume (SV), cardiac output (CO) and cardiac index (CI) during PAP titration in (1) in post-operative cardiac surgery patients, (2) patients with severe OSA, and (3) normal healthy volunteers.

Methods:
Post-operative cardiac surgery patients were studied via TEB and PAC during acute titration of positive end-expiratory pressure (PEEP) while mechanically ventilated. Patients with severe OSA were studied non-invasively by TEB during acute CPAP titration in supine stage 2 sleep, and normal subjects while awake and recumbent.

Results:
In three post-operative cardiac surgery patients, increasing PEEP to 18 cmH2O reduced SV by 13.8 +/- 2.0% (P = 0.0003) and CI by 12.0 +/- 1.9% (P = 0.0004) relative to baseline. There was no statistical difference between TEB and PAC in terms of ability to assess variations in hemodynamic parameters. In patients with severe OSA (n=3), CPAP titration to optimal pressure to alleviate obstructive apneas (median 8 cmH2O, range 5-9 cmH2O) reduced HR significantly from 71.9 +/- 3.9 min⁻¹ to 61.8 +/- 6.3 min⁻¹ (P < 0.0001); SV from 93.5 +/- 7.8 mL to 82.9 +/- 11.2 mL (P < 0.0001), CO from 6.7 +/- 0.7 L/min to 5.1 +/- 0.8 L/min (P < 0.0001) and CI from 2.9 +/- 0.3 L/min/m² to 2.3 +/- 0.4 L/min/m² (P <0.0001) compared to without CPAP but in the absence of apneas. In three healthy subjects, maximal tolerated CPAP (median 16 cmH2O, range 14-18 cmH2O) reduced SV and CO by 10.3% +/- 0.4% and 13.0% +/- 9.9% respectively when compared to baseline.

Conclusion:
Acute administration of CPAP causes a decrease in CO and CI, apparently a consequence of a reduction in SV. TEB appears to be an accurate and reproducible non-invasive method of detecting changes in hemodynamics, rendering it a suitable alternative to PAC in measuring hemodynamic parameters in patients on PAP therapy.

This abstract is funded by: No funding for project. Submitting author received the Heart & Stroke Foundation of Ontario (HSFO) Summer Medical Student Award for undertaking the project Am J Respir Crit Care Med 181;2010:A4541
Resistant Hypertension Comparing Hemodynamic Management to Specialist Care

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Abstract:
Although resistant hypertension affects a minority of all hypertensives, this group continues to experience disproportionately high cardiovascular event rates despite newer antihypertensive agents. Hypertension represents an imbalance of hemodynamic forces within the circulation, usually characterized by elevated systemic vascular resistance. We studied the utility of serial hemodynamic parameters in the selection and titration of antihypertensive medication in resistant hypertensive patients using highly reproducible noninvasive measurements by thoracic bioimpedance. Resistant hypertension patients (n=104) were randomized to drug selection based either on serial hemodynamic (HD) measurements and a predefined algorithm or on drug selection directed by a hypertension specialist (SC) in a 3-month intensive treatment program. Blood pressure was lowered by intensified drug therapy in both treatment groups (169±3/87±2 to 139±2/72±1 mm Hg HD versus 173±3/91±2 to 147±2/79±1 mm Hg SC, P<0.01 for systolic and diastolic BP), using similar numbers and intensity of antihypertensive medications. Blood pressures were reduced further for those treated according to hemodynamic measurements, resulting in improved control rates (56% HD versus 33% SC controlled to ≤140/90 mm Hg, P<0.05) and incremental reduction in systemic vascular resistance measurements. Although the number of patients taking diuretics did not differ between groups, final diuretic dosage was higher in the hemodynamic cohort. Our results demonstrate superior blood pressure control using a treatment algorithm and serial hemodynamic measurements compared with clinical judgment alone in a randomized prospective study. Our measurements of thoracic fluid volume support occult volume expansion as a mediator of antihypertensive drug resistance and use of impedance measurements to guide advancing diuretic dose and adjustment of multidrug antihypertensive treatment.

Keywords:
• Hypertension
• Resistant
• Hemodynamics
• Drug therapy
• Cardiography

IMPORTANT NOTE FROM THE MANUFACTURER:
The device used for this study was a standard impedance cardiograph device.
### Effects of sauna alone and post-exercise sauna baths on blood pressure and hemodynamic variables in patients with untreated hypertension.

_AQSAP, 19th March 2011_

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**Purpose:**
The aim of our study was to measure the effects of sauna alone (S) vs. exercise and sauna (ES) on blood pressure (BP) and central hemodynamic variables during and after sauna exposure in patients with untreated hypertension.

**Methods:**
16 untreated hypertensive subjects (61±9 years) were randomly assigned to 3 conditions: a resting control period (C), ES (30-min ergocycle exercise at 75% HRmax followed by two successive saunas) and S (two successive 8 min-sauna). Manual BP and hemodynamic measurements (cardiac bioimpedance, PhysioFlow®) were performed at baseline, during the 2 saunas (for ES and S), 15 and 120 min after saunas. 24h-ambulatory BP (ABP, Spacelabs®) was installed 120 min after sauna.

**Results:**
ES decreased ABPM daytime SBP, 24h-SBP (-5 mmHg, p<0.05) and 24-h mean BP. During sauna, SBP decreased at 2nd min of the 1st sauna (p<0.05) for S and ES. During saunas, HR and cardiac output increased (p<0.0001) for S and ES conditions, whereas ventricular ejection time and total vascular resistance (TVR) decreased (p<0.0001). End-diastolic volume increased in S and ES after 120 min (p<0.0001). TVR was reduced after 15 and 120 min for S and ES compared to C (p<0.0001).

**Conclusion:**
Exercise and sauna have positive effects on daytime and 24h SBP in patients with untreated hypertension on contrary to sauna alone. Exercise and sauna or sauna alone reduces TVR, with positive effects lasting 120 min after heat exposure. Exercise and sauna could be recommended as a non-pharmacological intervention for hypertension.
On- and off-exercise kinetics of cardiac output in response to cycling and walking in COPD patients with GOLD Stages I-IV.

Abstract:
Exercise-induced dynamic hyperinflation and large intrathoracic pressure swings may compromise the normal increase in cardiac output (Q) in Chronic Obstructive Pulmonary Disease (COPD). Therefore, it is anticipated that the greater the disease severity, the greater would be the impairment in cardiac output during exercise. Eighty COPD patients (20 at each GOLD Stage) and 10 healthy age-matched individuals undertook a constant-load test on a cycle-ergometer (75% WR(peak)) and a 6min walking test (6MWT). Cardiac output was measured by bioimpedance (PhysioFlow, Enduro) to determine the mean response time at the onset of exercise (MRTon) and during recovery (MRToff). Whilst cardiac output mean response time was not different between the two exercise protocols, MRT responses during cycling were slower in GOLD Stages III and IV compared to Stages I and II (MRTon: Stage I: 45±2, Stage II: 65±3, Stage III: 90±3, Stage IV: 106±3s; MRToff: Stage I: 42±2, Stage II: 68±3, Stage III: 87±3, Stage IV: 104±3s, respectively). In conclusion, the more advanced the disease severity the more impaired is the hemodynamic response to constant-load exercise and the 6MWT, possibly reflecting greater cardiovascular impairment and/or greater physical deconditioning.
Hemodynamic parameters in preeclampsia measured by transthoracic cardiac impedancemetry in the third trimester of pregnancy: An observational pilot study

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Introduction:
During preeclampsia, symptoms and signs are often late in this disease’s history, and the challenge is its early diagnostic, resulting early therapy, and consequently a lower morbidity and mortality. Nowadays, no per partum test is enough sensitive or specific to diagnose preeclampsia before the clinical signs appearance.

Transthoracic Cardiac impedancemetry (TCI) is a totally non invasive technique measuring systolic ejection volume (SEV), and calculating cardiac output (CO, cardiac index CI) and indexed systemic vascular resistances (ISVR), which could be interesting in the early detection of abnormal hemodynamic state in preeclampsia. The purpose of our study was to describe the variations of hemodynamic variables in preeclampsia during the third trimester of pregnancy using TCI in supine (S), left lateral (LL) and right lateral (RL) position, compared with non preeclamptic pregnant women, and non pregnant women.

Methods:
We conducted a prospective observational case control study. We included pregnant volunteer or with isolated pregnancy related hypertension women in the third trimester between the 32th and the 36th week of gestational age and divided them depending of their prognosis on term (preeclampsia, PE group, or eutocic birth, EUT group). We compared these patients, with 10 non pregnant women SUPINE, 15 minutes LEFT, 15 minutes RIGHT, 15min (TEM group). We measured by plethysmography and TCI (Physioflow ®, Manatec) for every women, systolic blood pressure, diastolic and average blood pressure, CO, cardiac index (CI), ISVR. The measures were during 15 minutes in strict S, then the measures were repeated. We calculated the difference between each position sequence for every parameter. After the measures, the patients were followed until the 15 days postpartum and distributed according to their prognosis.

Results:
We included 10 patients per group. The TCI was performed at 35 SA for the EUT and PE group. The median term was 40 amenorrhea weeks (AW) in the EUT group and 36,6 AW in the PE group.

7 patients on 10 of the PE group had a negative cardiac index variation when changing from supine to lateral position (left or right) vs 2 in the EUT group. The principal hemodynamic variables between group is described in the following table (*= p<0,05, median [extremes])

<table>
<thead>
<tr>
<th>Parameter/position</th>
<th>EUT (n=10)</th>
<th>PREECLAMPSIA (n=10)</th>
<th>NON PREGNANT(n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indexed Cardiac output/ Supine</td>
<td>3,5 [2,7-4,5]</td>
<td>3 [1,6-3,6]</td>
<td>3,3 [2,8-4]</td>
</tr>
<tr>
<td>Cardiac output/ Left Lateral</td>
<td>3,4 [2,6-4,4]</td>
<td>*2,4 [1,8-3,3]</td>
<td>2,9 [2,5-3,3]</td>
</tr>
<tr>
<td>Indexed Systemic vacular resistances/Supine</td>
<td>1894[1050-2790]</td>
<td>*3376[2523-7018]</td>
<td>2142 [1730-2409]</td>
</tr>
<tr>
<td>Indexed Systemic vacular resistances/Left Lateral</td>
<td>1687[1197-3617]</td>
<td>*3382 [2463-3971]</td>
<td>2345 [2128-2668]</td>
</tr>
<tr>
<td>Cardiac index variations between Supine and LL % [+ SEM] . p=0,3</td>
<td>0,98 [-4,31]</td>
<td>-7,39 [+7,3]</td>
<td>-10,9 [+ 4,92]</td>
</tr>
</tbody>
</table>

Conclusion:
In preeclampsia, high RVSI have already been described in several studies. Theses RVSI don’t significantly change when the patient changes his position from SUPINE to LATERAL POSITION, but CO and CI do. Moreover, the CI and RVSI achieve the levels found in the litterature in preeclamptic patients. CO measurement with Physioflow® TCI device seems well correlated with CO measurement thermodilution technics (1) in the litterature. In our study, variation of cardiac index (measured with TIC) during changes of position between SUPINE to RIGHT OR LEFT position measured at 35 SA, could have a high prognostive power for an evolution toward preeclampsia. Our study is limited by our cohort’s smallness. Further studies are needed to conclude discriminative power of the delta IC in the diagnostic of PE.

We have already started a new study comparing cardiac output correlation between transthoracic echocardiography and TCI in third trimester pregnant and non preeclamptic, which are nowadays, missing data, to validate TCI in these patients. Furthermore we are still including patients in a larger cohort study, allowing more focused search on relations between known prognosis factors, prognosis and hemodynamic parameters measured by TCI.
Determination of Hemodynamic Parameters During 6-Minute Walk Test In Pulmonary Hypertension

Authors: Vineesha Arelli MD, Jose Ramos RRT, Kevin McCarthy RPFT, Adriano Tonelli MD, Raed A. Dweik MD, Adriano R. Tonelli MD

Cleveland Clinic, Cleveland, Ohio, USA

Background:
- Pulmonary hypertension (PH) is a disease, characterized by an increase in pulmonary pressures, ultimately leading to right heart failure and death.
- The diagnosis and management of PH requires right heart catheterization (RHC). Impedance cardiography is a noninvasive methodology that determines resting cardiac output with good accuracy and fair precision in patients with PH.
- Objective functional capacity in this disease is commonly assessed by the six-minute walk test (6MWT), a study that provides information on disease severity, prognosis and response to therapy.
- No previous studies have assessed the cardiac output response during 6MWT in PH using impedance cardiography.

Methods:
- Patients with PH, confirmed with RHC, were recruited at the time of their 6MWT.
- We used a new generation portable impedance cardiography device (Physioflow enduro, Manatec Biomedical, Paris, France) with real time wireless monitoring via a bluetooth USB adapter.
- Physioflow measures changes in transthoracic impedance in response to the administration of a high frequency and low-amperage alternating electrical current via skin electrodes.
- We determined heart rate (HR), stroke volume (SV), cardiac output (CO) and cardiac index (CI) before, during and for three minute after the 6MWT.

Results:
- We included 18 patients (61% female), mean (SD) age 51.4 (16) years.
- Pulmonary arterial hypertension was present in 78% of patients. The rest had chronic thromboembolic PH or PH associated with parenchymal lung disease. All but 3 patients were on PH-specific therapies.
- Baseline HR is inversely associated with SV at baseline (r = -0.7, p < 0.001) and at its peak (r = -0.48, p = 0.04).
- Similarly, maximum HR is inversely associated with SV at baseline (r = -0.75, p <0.001) and at its peak (r = -0.56, p = 0.017).
- The CO acceleration slope is associated with peak CO (r = 0.72, p < 0.001) and distance walked in meters (r = 0.49, p = 0.039)
- Peak CO is significantly associated with maximal SV (r = 0.66, p = 0.003) but not maximal HR ( r = 0.2, p = 0.38) on univariable linear regression analysis.

Conclusion:
- Real time wireless impedance cardiography allows the non-invasive determination of hemodynamic parameters in PH patients during 6MWT.
- SV, CO and CI increase with activity. CO acceleration slope is directly associated with the distance walked and peak CO.
- The addition of impedance cardiography to the 6MWT can potentially increase the value of this test and provide insight into the hemodynamic changes during exercise in PH.
Signal morphology impedance cardiography during incremental cardiopulmonary exercise testing in pulmonary arterial hypertension.

Clin Physiol Funct Imaging

Authors:
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• Célia Maria C Silva,
• Luiz Eduardo Nery,
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Abstract:
Haemodynamic responses to exercise are related to physical impairment and worse prognosis in patients with pulmonary arterial hypertension (PAH). It is clinically relevant, therefore, to investigate the practical usefulness of non-invasive methods of monitoring exercise haemodynamics in this patient population.

Using a novel impedance cardiography (ICG) approach that does not require basal impedance estimations and relies on a morphological analysis of the impedance signal (Signal-Morphology-ICG™)), stroke volume (SV) and cardiac index (CI) were evaluated in 50 patients and 21 age-matched controls during a ramp-incremental cardiopulmonary exercise testing. Technically unacceptable readings were found in 12 of 50 (24%) patients. In the remaining subjects, early decrease (N = 9) or a 'plateau' in SV (N = 8) and Δ (peak-unloaded exercise) SV <10 ml were markers of more advanced PAH (P<0.05). ΔCI ≤ 1.5-fold and early estimated lactate threshold were the only independent predictors of a severely reduced peak oxygen uptake (VO(2)) in patients (R(2) = 0.71, P<0.001). The finding of ΔCI ≤ 1.5-fold plus peak VO(2) <50% predicted was associated with a number of clinical and functional markers of disease severity (P<0.001). In addition, abnormal SV responses and ΔCI ≤ 1.5-fold were significantly related to 1-year frequency of PAH-related adverse events (death and balloon atrial septostomy, N = 8; P<0.05).

‘Qualitative’ and ‘semi-quantitative’ signal-morphology impedance cardiography(™) (PhysioFlow(™)) during incremental exercise provided clinically useful information to estimate disease severity and short-term prognosis in patients with PAH in whom acceptable impedance signals could be obtained.
Persistent elevation of central pulse pressure during postural stress in patients with type 2 diabetes mellitus

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Abstract:
An abnormal increase or decrease in blood pressure (BP) in response to postural stress is associated with increased risk of developing hypertension and stroke. However, the haemodynamic responses contributing to changes in central BP with postural stress are not well characterised. We aimed to determine this in controls compared to patients with type 2 diabetes mellitus (T2DM), whom we hypothesised would have an abnormal postural response. 41 participants (20 control, 21 T2DM) underwent measurement of brachial and central BP (by radial tonometry), with simultaneous bioimpedance cardiography (to determine stroke volume (SV) and cardiac output (CO)) and heart rate variability in seated and standing postures. Systemic vascular resistance (SVR; mean arterial pressure/CO), and arterial elastance (EA; end systolic pressure/SV) were calculated. Postural changes were defined as seated minus standing values. Central pulse pressure (PP) was higher in patients with T2DM and did not change from seated-to-standing positions, whereas there was a significant decrease upon standing in controls (Po0.05). The change in central systolic BP (SBP) correlated with change in SVR and EA in controls (r=0.67 and 0.68, Po0.05, respectively), but not in patients with T2DM (r=-0.05 and r=0.03, P>0.05, respectively). SV was the only significant correlate of change in central SBP in T2DM patients (r=0.62, Po0.05) and this was not observed in controls (r=0.08 P=0.05). We conclude that central haemodynamic responses to postural stress are altered in patients with T2DM and result in persistent elevation of central PP while standing. This may contribute to increased cardiovascular risk associated with T2DM.

Keywords:
• haemodynamics,
• type 2 diabetes,
• pulse wave analysis,
• posture.
Hemodynamic effects of high intensity interval training in COPD patients exhibiting exercise-induced dynamic hyperinflation.


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Abstract:
Dynamic hyperinflation (DH) has a significant adverse effect on cardiovascular function during exercise in COPD patients. COPD patients with (n=25) and without (n=11) exercise-induced DH undertook an incremental (IET) and a constant-load exercise test (CLET) sustained at 75% peak work (WRpeak) prior to and following an interval cycling exercise training regime (set at 100% WRpeak with 30-s work/30-s rest intervals) lasting for 12 weeks. Cardiac output (Q) was assessed by cardio-bio-impedance (PhysioFlow, enduro, PF-O7) to determine Q mean response time (QMRT) at onset (QMRTOS) and offset (QMRTOFF) of CLET. Post-rehabilitation only those patients exhibiting exercise-induced DH demonstrated significant reductions in QMRTOS (from 82.2±4.3 to 61.7±4.2s) and QMRTOFF (from 80.5±3.8 to 57.2±4.9s). These post-rehabilitation adaptations were associated with improvements in inspiratory capacity, thereby suggesting that mitigation of the degree of exercise-induced DH improves central hemodynamic responses in COPD patients.

Keywords:
• COPD
• Cardiac output
• Pulmonary rehabilitation

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Effect of Pulmonary Rehabilitation on Cardiac Output Responses during Exercise in COPD


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Abstract:

Introduction: In patients with COPD pulmonary rehabilitation (PR) induces true physiological effects reflected by reduced ventilatory requirement and improved peripheral muscle function. The effect of PR on central hemodynamic responses during exercise remains largely unknown.

Aim: To examine the impact of PR on cardiac output (Q) responses during incremental (IE) and constant-load exercise (CLE).

Method: 60 COPD patients (GOLD stages II-IV) were studied (including 15 controls). PR consisted of interval cycling exercise 3 days/week for 10 weeks, with 30-s work periods/30-s rest periods for 30 min/day and intensity at 100% of peak work capacity (Wpeak). Q was measured by bio-impedance (Physioflow PF-O7) during IE and CLE at 75% Wpeak for 6-min during exercise and in recovery, prior to and following PR.

Results: At Wpeak there was an increase in Q after PR (from 10.1±0.5 to 12.4±0.6, L/min, p=0.001) due to increased SV (from 90±3.2 to 105.1±4.42 ml/min, p=0.003). Post-rehabilitation at an identical work rate during IE, Q did not differ compared to pre-rehabilitation; however SV was higher (pre: 90±3.2; post 95±3.2 ml/min) and HR lower (pre: 113±3; post 106±3 beats/min, p=0.008). Postrehabilitation during CLE there were significant reductions in Q mean response time (MRT) at the onset and offset of exercise (pre: 79.8±4.4; post: 66.9±4.5sec, p=0.001) and (pre: 79.1±4.3, post: 66.1±4.2 sec, p=0.001), respectively.

Conclusion: Pulmonary rehabilitation induces an improvement in central hemodynamic function to incremental and constant-load exercise in patients with COPD across GOLD stages II to IV.
The Higher the Insulin Resistance the Lower the Cardiac Output in Men with Type 1 Diabetes During the Maximal Exercise Test

Metabolic Syndrome and related Disorders 2017, 15 (5): 252-257

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Abstract:
BACKGROUND: The aim of this study was to assess the hemodynamic parameters analyzed in bioimpedance cardiography during maximal exercise in patients with type 1 diabetes differing in insulin resistance.

METHODS: The study group consisted of 40 men with type 1 diabetes. Tissue sensitivity to insulin was assessed on the basis of the glucose disposal rate (GDR) analyzed during hyperinsulimemic-euglycemic clamp. Patients were divided into groups with GDR <4.5 mg/kg/min (G1 group-lower insulin sensitivity) and GDR ≥4.5 mg/kg/min (G2 group-higher insulin sensitivity). During the exercise test, the heart rate, systolic volume, cardiac output, cardiac index were measured by the impedance meter (PhysioFlow).

RESULTS: Compared with the G2 group, the G1 group had a lower cardiac output (CO): during exercise 8.6 (IQR 7.7-10.0) versus 12.8 (IQR 10.8-13.7) L/min; P < 0.0001, at the maximal effort 13.1 (IQR 12.2-16.7) versus 18.6 (IQR 16.9-20.2) L/min; P = 0.001, and during observation after exercise 8.4 (IQR 6.3-9.6) versus 11.9 (IQR 10.1-13.1) L/min; P < 0.0001. We noticed a positive correlation of GDR and cardiac output: during the exercise test (r = 0.63, P = 0.0002), at the maximal effort (R = 0.56, P = 0.001), and during observation after the exercise test (r = 0.72, P < 0.0001). In multivariate logistic regression, cardiac output during exercise and during observation was associated with high GDR, regardless of the age and duration of diabetes [OR: 1.98 (95% CI 1.10-3.56), P = 0.02 and OR: 1.91 (95% CI 1.05-3.48), P = 0.03; respectively].

CONCLUSION: In nonobese subjects with type 1 diabetes, with good metabolic control, insulin resistance is associated with cardiac hemodynamic parameters assessed during and after exercise. The higher the insulin resistance the lower the cardiac output during maximal exercise in men with type 1 diabetes.
Management of an LCHADD Patient During Pregnancy and High Intensity Exercise

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Abstract:
In this report we describe a female Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHADD) patient who suffered from severe exercise intolerance. At age 34, the patient became pregnant for the first time. After an uneventful first 32 weeks of pregnancy she developed sinus tachycardia (resting heart rate 120–134 bpm) and lactate and creatinine kinase levels increased (3.3 mmol/L and 264 U/L, respectively). Increasing MCT supplementation (dose and frequency of administration) lowered heart rate and improved biochemical parameters. At 34 weeks the heart rate rose again and it was decided to deliver the child by caesarean section. Postpartum both mother and child did well. Prior to pregnancy, she performed exercise tests with different doses of medium chain triglycerides (MCTs) to establish a safe and effective exercise program (baseline test, second test with 10 g MCTs and third test with 20 g of MCTs). In the MCT supplemented tests the maximal power output was 23% (second test) and 26% (third test) higher, while cardiac output at maximal power output was the same in all three tests (~15.8 L/min). In conclusion, this is the first report of pregnancy in an LCHADD patient, with favourable outcome for both mother and child. Moreover, in the same patient, MCT supplementation improved cardiac performance and metabolic parameters during high intensity exercise. Using impedance cardiography, we got a clear indication that this benefit was due to improved muscle energy generation at high intensity exercise, since at the same cardiac output a higher power output could be generated.
SILDENAFIL RESTORES THE HEMODYNAMIC RESPONSE DURING MAXIMAL EXERCISE IN PATIENTS WITH CYSTIC FIBROSIS

Supported in part by a Vertex Pharmaceuticals IIS and NIH/NIDDK R21DK100783 (RAH).

Abstract:
It is well established that patients with cystic fibrosis (CF) exhibit exercise intolerance; however, the mechanisms have yet to be elucidated. We have documented vascular dysfunction at rest in patients with CF and therefore, it is conceivable that the hemodynamic response is compromised during exercise in this patient population. Sildenafil is a phosphodiesterase type 5 inhibitor that promotes arterial vasodilation resulting in enhanced blood flow.

Purpose: To explore the hemodynamic response during maximal exercise in patients with CF and controls, and determine if a single dose of sildenafil improves this response in patients with CF.

Methods: Hemodynamic variables were collected in 19 patients with CF (20 ± 2 years) and 15 controls (26 ± 2 years) at baseline and throughout a maximal exercise test on a cycle ergometer. Six of the patients also performed maximal exercise testing 1 hour following ingestion of a single dose of sildenafil (50 mg; CF-SIL). Hemodynamic parameters were assessed using Physioflow Enduro and included cardiac output (CO), left cardiac work index (LCWI), and systemic vascular resistance (SVR) among many others.

Results: Cardiac output (p=0.048) and LCWI (p=0.015) were significantly lower at baseline in patients with CF compared to controls. A significant group by time interaction (F1,32 = 9.497; p=0.004) for SVR was observed. Specifically, SVR at baseline was significantly (p=0.018) higher in CF (1599 ± 92 dyn.s/cm5) compared to controls (1307 ± 60 dyn.s/cm5). Additionally, there was a greater drop (p=0.004) in SVR from baseline to maximal exercise in patients compared to controls (-924 ± 72 vs. -639 ± 51 dyn.s/cm5, respectively). Following sildenafil, no difference (p=0.332) in the change in SVR from baseline to maximal exercise was observed between CF-SIL (-549 ± 65 dyn.s/cm5) and controls (-639 ± 51 dyn.s/cm5). Additionally, baseline CO (p=0.382) and LCWI (p=0.717) were similar between CF-SIL and controls.

Conclusion:
These data indicate that patients with CF have compromised hemodynamic function at rest and exhibit an exaggerated reduction in systemic vascular resistance during maximal exercise. In addition, a single dose of sildenafil in CF appears to restore the systemic vascular resistance response to maximal exercise. Future studies are warranted to determine the contribution of the hemodynamic response to exercise intolerance in this patient population.
2.3 INTENSIVE CARE

Advances in Non-invasive Cardiac Output Monitoring

*Annals of Cardiac Anaesthesia 2002;5:141-148*

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**Abstract:**

In EIC (Electrical Impedance Cardiographs) devices using Zo baseline impedance, large amounts of thoracic fluid may interfere with the impedance signal, making haemodynamic data unattainable or unreliable. Severe pulmonary edema may decrease the signal-to-noise ratio, damp the dZ/dt waveform, and inhibit haemodynamic data acquisition. The latest methods of EIC (PhysioFlow®) are baseline impedance independent and use more advanced forms of impedance waveform morphology analysis. New noninvasive impedance monitors are able to provide continuous trend monitoring of HR and SV giving derived CO and index parameters without the need for baseline impedance measurement. They use stroke waveform morphology analysis to determine SV and then calculate all the derived parameters. Preload assessment is essential in any patient who may be at a risk of hypoperfusion. Assessment and management of preload catheter can be a challenge for clinicians. The insertion of a CVP catheter may help decision making but isolated measurements of CVP are not very informative. The trend of the CVP and in particular its response to a fluid challenge is far more valuable in planning the therapy. In PA catheterisation, the PAOP indirectly measures LV end-diastolic pressure and is related to LV end-diastolic volume, or preload. However, many factors affect the extrapolation of the PAOP to LV preload, such as reduced LV compliance, pulmonary hypertension or mechanical ventilation. A simple manoeuvre using EIC to assess intravascular volume is to give a fluid challenge using the patient’s own circulating volume as the fluid bolus. By elevating the legs or placing the patient in the "head clown" position, fluid moves from the lower extremities, increasing venous return. In a normal heart, the SV will increase. Patients who are hypovolaemic may show a significant increase in SV and would benefit from volume administration. Patients with LV dysfunction or fluid overload may have minimal or no change in SV in response to a physiologic fluid bolus. These individuals do not have adequate cardiac reserve and cannot tolerate additional fluid. These patients may require treatment with inotropes or agents that reduce preload and afterload. Use of EIC to assess preload with a fluid affords valuable information regarding the patient’s ability to tolerate additional fluids. The latest methods of El use advanced waveform morphology analysis to determine a filling index (FI) for the heart. Where CVP measurements are available the information can be used to supplement the FI data. The trend of the FI is likely to be of more value than isolated measurements particularly for monitoring response to interventions or planning therapy.

**Conclusion:**

Recent technological advances have allowed the development of noninvasive methods of measuring CO with continuous on-line measurement and trending of SV and HR. Derived parameters such as SVI, CI, SVR, LCWI and EF can also be shown and recorded continuously. The new noninvasive technology is safe, reliable and relatively inexpensive and is increasingly being used in clinical practice and research. Completely noninvasive CO monitoring by modern EIC technology is suitable for continuous on-line and trend monitoring of SV, HR and derived parameters; and echocardiography, mainly TEE in the ICU, should be used for structural and functional evaluation of the heart as well as confirmation of SV and EF.
Hemodynamic Responses of a Spontaneous Breathing Trial Monitoring by an Impedance Cardiograph

Accepted by the American Thoracic Society, May 17-22, 2002

Authors:
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Introduction:
Left ventricular insufficiency is a common cause of ventilator weaning failure. We evaluated the hemodynamic parameters during a T-piece trial.

Methods
We conducted a prospective, open study in an intensive care unit. Heart rate (Hr), stroke volume (SV) and cardiac index (Ci) measurements were performed by PhysioFlowTM in ventilated adults ready for weaning. Patients with a SaO2>90% while breathing with a FiO2 of 40% or less, a PEEP<5cmH2O, a hemoglobin level above 8g/dl and without electrolyte disorders were included. Patients with inotropic drugs, altered mental status or pregnant women were excluded. We assessed the cardiac function during mechanical ventilation (MV) and during a T-piece trial of 30 minutes (SV). If a patient had any signs of poor tolerance during the trial the mechanical ventilation was reinstituted. Comparison of continuous variables was done with Student’s T-test. A p value under 0.05 was considered as significant. Results are expressed as mean +/- standard error.

Results:
7 patients were included and 10 trials were executed. The rate of success was 70%. Three patients failed the trial (two met the criteria of a respiratory distress (respiratory frequency greater than 30/min) and one altered his Glasgow score. For the patients with a respiratory distress the Hr (108 +/- 11 bpm vs 108 +/- 15 bpm), SV (73 +/- 10 ml vs 89 +/- 16 ml) and Ci (4.5 +/- 1.5 l/min.m2 vs 5.6 +/- 2.1 l/min.m2) were unchanged during SV compared with MV. For the other patients Hr increased from 85 +/- 21 bpm to 90 +/- 19 bpm (p<0.05), SV dropped from 80 +/- 10 ml to 72 +/- 14 ml (p<0.05) and Ci was unchanged with 3.5 +/- 0.7 vs 3.3 +/- 0.6 l/min.m2.

Conclusion:
We showed that the hemodynamic consequences of a spontaneous breathing trial was a decrease of SV for the patients without signs of respiratory distress. Thoracic bioimpedance could be a good tool for the hemodynamic assessment during ventilator weaning.
Non-invasive Haemodynamic Monitoring to Predict Outcome and Guide Therapy in Acute Critical Illness

International Journal of Intensive Care, Spring 2007

Authors: • William Shoemaker, MD.

Abstract-aim: To compare invasive pulmonary artery catheter (PAC) data with continuous noninvasive haemodynamic monitoring using a program to predict outcome and guide therapy beginning shortly after emergency department (ED) admission in a university-run inner city public hospital.

Methods: We compared PAC data with noninvasive monitored: cardiac function by cardiac output (CI), mean arterial blood pressure (MAP), and heart rate (HR); respiratory function by arterial oxygen saturation (SapO2); tissue perfusion/oxygenation by transcutaneous tensions of CO2 and O2 indexed to FIO2. A search and display program calculated survival probabilities (SP) and a decision support program predicted effects of various therapies.

Results: Survivors’ MAP, CI, SapO2, and PtcO2/FIO2, and SP were significantly higher (p <0.05) than nonsurvivors’ values in each diagnostic category.

Conclusion: Compared with the PAC, noninvasive monitoring is safer, simpler, easier, quicker, cheaper, reasonably accurate, and available anywhere in the hospital or prehospital areas. Increased CI and tissue oxygenation determined by the distribution of metarteriolar flow are underlying haemodynamic patterns associated with survival.
The changing Hemodynamic Parameters during weaning from mechanical ventilation

**Authors:**
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**Abstract-Background:**
Several weaning parameters have been broadly used for prediction the probability of weaning. Spontaneous breath trial does, too. However, there still some patients (pts) well tolerate T-piece for 2hrs, but fail to wean from mechanical ventilation (MV). Hemodynamic conditions have been though one of the reasons of weaning failure. Do they really affect the result of weaning?

**Methods:**
A prospective study in medical ICU in patients (pts) meeting the criteria for weaning was analyzed the hemodynamic parameters, including ejection fraction (EF), stroke volume (SV), heart rate (HR), cardiac out (CO) and cardiac index (CI) during 2hr-spontaneous breath trial. Nineteen pts were included between Oct 2004 and Jan 2006, in Mackay Memorial Hospital, Taiwan. All the hemodynamic data were collected by Physio flow.

**Results:**
Ten pts succeeded to wean, and nine pts failed. In success group, the CI (l/min/m2), CO (l/min), SV (ml), and HR (bpm) presented fine fluctuation. In failure group, CI (l/min/m2), CO (l/min), SV (ml), and HR (bpm) increased persistently during spontaneous breath trial. All pts did not show oxygen desaturation. (The initial and last CI (l/min/m2) during 2 hr-spontaneous breath were 3.75 and 3.69; CO (l/min) 4.97 and 4.91; SV (ml) 54.53 and 54.01; HR (bpm) 91.99 and 93.05 in success group. In failure group, the initial and last CI (l/min/m2) during 2 hr-spontaneous breath were 3.82 and 4.66; CO (l/min) 6.36 and 7.79; SV (ml) 63.50 and 69.34; HR (bpm)100.55 and 109.93.) The trends of hemodynamic parameters have been shown in figures.

**Conclusion:**
1. Increasing oxygen demand during weaning from MV will be compensated by cardiac performance. However, persistent increasing cardiac work may result in failure of weaning.
2. Monitoring the hemodynamic parameters during spontaneous breath trial may be a tool to avoid unnecessary muscle fatigue.
2. Application studies
2.3 Intensive Care

Thoracic electrical bioimpedance: a tool to determine cardiac versus non-cardiac causes of acute dyspnoea in the emergency department


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**Objectives:**
To determine whether cardiohaemodynamic parameters, using non-invasive thoracic electrical bioimpedance (TEB), can differentiate between cardiac and non-cardiac causes of acute breathlessness in adult emergency department (ED) patients.

**Methods:**
A prospective cohort study of adult patients who presented with acute breathlessness to the ED of a large urban teaching hospital. Study patients had their cardiohaemodynamic parameters measured, using a TEB device. The patient’s hospital discharge diagnosis was used as the definitive diagnosis to determine whether the underlying cause of acute dyspnoea was cardiac or non-cardiac related. The definitive diagnosis was compared with the TEB data and the ED physician’s diagnosis.

**Results:**
52 patients were recruited into the study, of whom 51 had complete TEB data and were included in the analysis. There were statistically significant differences in cardiac output (6.2 vs 7.9, p<0.001), cardiac index (CI; 3.1 vs 4.4, p<0.001), systemic vascular resistance (1227 vs 933, p=0.002) and systemic vascular resistance index (2403 vs 1681, p<0.001) between the cardiac and non-cardiac cohort. CI was found to be an excellent discriminator (receiver operating characteristics area under the curve 0.906). The optimal diagnostic criterion for CI to distinguish between cardiac and non-cardiac dyspnoea was 3.2 l/min per square metre or less (positive likelihood ratio 7.9; negative likelihood ratio 0.14).

**Conclusion:**
This study demonstrated that non-invasive TEB cardiohaemodynamic parameters can differentiate between cardiac and non-cardiac-related causes of dyspnoea in ED patients presenting with acute breathlessness. A large-scale trial is required to determine if TEB-derived cardiohaemodynamic information can aid ED clinicians in their early clinical decision-making and improve the care and outcome of patients with dyspnoea.
2.4 ANESTHESIA

Decreased Cardiovascular Hemodynamics as Possible Mechanisms of Hypotension during Cesarean Delivery under Spinal Anesthesia: Role of Thoracic Impedance Cardiography

Society of Obstetrics Anesthesiology and Perinatology (SOAP), March 2008

Authors:
• Nico Terblanche, MD, FCA (SA); Bruno Borges, MD; Jose C.A. Carvalho, MD, PhD, FANZCA, FRCPC; Kong E. You-Ten, MD, PhD, FRCPC

Abstract-Background:
Maintaining normal blood pressure in pregnant patients is important for normal placental blood flow and to avoid undesirable symptomatic adverse effects such as nausea and vomiting. Despite our practice to maintain normal baseline blood pressure with phenylephrine, an α1-agonist, hypotension remains the most common complication during Cesarean delivery under spinal anesthesia. A decrease in cardiac output as a result of decreased preload, and a decrease in systemic vascular resistance from spinal-induced sympathetic blockade are two mechanisms postulated to be responsible for the hypotension in this patient population. Other drugs used intra-operatively, such as oxytocin, may further compromise patient hemodynamics. Normal cardiovascular functions, including cardiac output, stroke volume, heart rate, and systemic vascular resistance, are known to maintain blood pressure. We propose that a continuous monitoring of these cardiovascular functions (ie. hemodynamics) may provide insights into the mechanism(s) of hypotension during a Cesarean delivery under spinal anesthesia.

Objectives:
In the present pilot study, we aim to (1) measure several cardiovascular hemodynamics continuously during elective Cesarean delivery under spinal anesthesia using noninvasive thoracic impedance cardiography, and (2) to determine whether these cardiovascular hemodynamics may be responsible for changes in blood pressure.

Methods:
With Institutional Research Ethics Board approval, and patients' informed consent, 10 ASA I and II patients undergoing elective Cesarean delivery under spinal anesthesia were observed in a prospective, nonrandomized, non-blinded observational cross-sectional pilot study. The Physioflow Impedance Device (VasoCom Inc, Philadelphia) was used to measure the cardiac index (CI), systemic vascular resistance (SVRI), stroke volume (SV), systolic blood pressure (SBP) and heart rate (HR). Baseline hemodynamics were measured before the spinal anesthesia. All patients were in a left lateral position with a wedge and standard anesthesia monitors were applied. Spinal anesthesia was then performed with 12.5 mg of 0.75% hyperbaric bupivacaine, 10 mcg fentanyl and 100 mcg morphine via a 27G Whittacre needle. Thereafter, hemodynamics were monitored every minute until completion of the surgical procedure. All patients were preloaded with 1000 ml of Lactated Ringers’ solution prior to the insertion of the spinal anesthesia. Phenylephrine at doses of 100-200
mcg bolus was the preferred treatment of hypotension with the aim to preserve systolic blood pressure at 100% of baseline. Repeated measures analysis of variance (ANOVA) was used to compare any differences from baseline controls, with p value < 0.05 to be statistically significant.

Results:
We were successful in measuring continuously several cardiovascular functions in all 10 patients until the completion of the Cesarean delivery. We observed the greatest change of the cardiovascular hemodynamics before and after delivery. Table 1 showed that the SBP before (98.3 ± 5.7) and after (98.3 ± 5.6) were significantly decreased by 25% when compared to baseline control (133 ± 5.6). In addition, all measured cardiovascular functions (CI, HR, SV, SVRI) were also significantly decreased before and after delivery.

Conclusion:
Despite a preventive approach using phenylephrine to maintain baseline blood pressure, significant hypotension still occurs during Cesarean delivery under spinal anesthesia. Our results suggest that significant decrease in several cardiovascular functions (CI, HR, SV, and SVRI) may be responsible for the occurrence of hypotension. In addition, thoracic impedance cardiography with the Physioflow Impedance device provides a reliable noninvasive monitoring of the cardiovascular hemodynamics. Thus, continuous monitoring of cardiovascular functions with noninvasive impedance may provide insights into the mechanisms of hypotension. This may lead to preemptive treatments before significant hypotension occurs and to avoid undesirable symptomatic effects. A larger study is further required to confirm these preliminary findings.

Table 1. Cardiovascular Hemodynamics Before and After Deliverya

<table>
<thead>
<tr>
<th>Hemodynamics Parameters</th>
<th>Baseline Control</th>
<th>Before Delivery</th>
<th>After Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>133 ± 5.6</td>
<td>98.3 ± 7.04</td>
<td>98.3 ± 5.7</td>
</tr>
<tr>
<td>CI</td>
<td>4.6 ± 0.32</td>
<td>2.9 ± 0.16</td>
<td>3.5 ± 0.31</td>
</tr>
<tr>
<td>HR</td>
<td>93.3 ± 3.0</td>
<td>63.1 ± 1.6</td>
<td>72.4 ± 3.6</td>
</tr>
<tr>
<td>SV</td>
<td>94.3 ± 5.48</td>
<td>79.7 ± 4.5</td>
<td>83.4 ± 5.7</td>
</tr>
<tr>
<td>SVRI</td>
<td>1823.2 ± 206.7</td>
<td>1336.5 ± 165.5</td>
<td>1224.2 ± 171.5</td>
</tr>
</tbody>
</table>

*All results before and after delivery were significant p < 0.05, when compared to control baseline.

References:
Tihtonen, K et al. BJOG 2006; 113, 657
Maternal haemodynamics at elective caesarean section: a randomised comparison of oxytocin 5-unit bolus and placebo infusion with oxytocin 5-unit bolus and 30-unit infusion


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**Background:**

Rapid intravenous injection of oxytocin is associated with marked hypotension secondary to decreased venous return. Reductions in dose and rate of bolus administration have reduced the incidence of cardiovascular side effects, but no study has yet investigated cardiovascular stability when oxytocin is infused for several hours after delivery. This study compared maternal haemodynamics during a 4-h 30-unit oxytocin infusion and during a placebo infusion following caesarean section.

**Methods:**

Women booked for elective caesarean section were randomised to receive either oxytocin 5-unit bolus and placebo infusion or oxytocin 5-unit bolus and oxytocin 30-unit infusion. Before, during and for 4 h after surgery electrocardiogram, oxygen saturation, systolic and diastolic pressure and heart rate were monitored non-invasively and cardiac index (CI), left ventricular work index (LVWi) and systemic vascular resistance index (SVRi) by thoracic bioimpedance.

**Results:**

A total of 74 women agreed to haemodynamic measurements. Heart rate, systolic and diastolic pressure, CI, LCWi and SVRi all fell following the onset of spinal anaesthesia, and, with the exception of SVRi, continued to decrease throughout surgery. After delivery of the baby, slow injection of oxytocin 5 units was associated with a temporary rise in CI, LCWi and heart rate, a decrease in SVRi and no change in systolic or diastolic pressure. Thereafter, haemodynamic measures returned to normal over 60 min with no adverse effects apparent from the additional oxytocin infusion.

**Keywords:**

- Maternal haemodynamics
- Caesarean section
- Oxytocin
- Bioimpedance

**Conclusion:**

An additional oxytocin infusion at elective caesarean section did not adversely affect maternal haemodynamics either during or after surgery.
## Introduction:

Les événements cardiovasculaires indésirables péri opératoires (ECVI) sont associés à une morbidité accrue à long terme (Anesthesiology 1996, 84 : 772-81). Le but de cette étude était d'identifier parmi les paramètres de cardio-impédancémétrie mesurés en préopératoire les facteurs prédictifs de survenue d'ECVI.

## Matériel & Méthodes:

Après avis d'un comité d'éthique et recueil d'un consentement éclairé, une mesure des paramètres de cardio-impédancémétrie (Physioflow®) a été réalisée en préopératoire chez 67 patients devant subir une anesthésie générale pour chirurgie abdominale ou vasculaire entre octobre et décembre 2005. Pendant l'intervention et pour chaque patient inclus, ont été rapportées par un médecin ne connaissant pas les paramètres d’impédance mesurés en préopératoire, la survenue ou non d’un ECVI (hypotension, hypertension, bradycardie, tachycardie, modification ST). La fréquence des ECVI a été notée et des comparaisons ont ensuite été effectuées entre l’ECVI le plus fréquent et les différents paramètres mesurés en préopératoire. Une ANOVA ou un test de Kruskal-Wallis ont été utilisés selon l'égalité de variance ou non.

## Résultats:

Les caractéristiques de l'échantillon étaient : âge moyen 65,3 ans, sex ratio M/F 2,5, score de Goldman 10 points, coronariens : 28 %, ASA ≥ 3 : 13 %. Une hypotension a été notée chez 48 % des patients, une HTA (10 %), une bradycardie (12 %). Une association significative a été notée entre la survenue d'une hypotension et les paramètres suivants : Fc (p=0,02), VES (p<0,05), RPD (indice de remplissage proto diastolique (p=0,014). La survenue d’une hypotension augmentait avec l’âge (p=0,05), et l’ICT (indice de contractilité) (NS : p=0,056). Il n’existait pas d’association significative entre l’hypotension et les paramètres suivants : index cardiaque, PAS, résistances indexées, TEV, IFT (eau intra thoracique).

## Discussion:

Bien qu’une conférence internationale propose un algorithme décisionnel sur le risque cardiovasculaire péri opératoire (J Am Coll Cardiol 2002, 39 : 542-53), l’appréciation de ce dernier reste difficile à apprécier, consommateurs de temps et parfois de moyens d’investigation agressifs. La cardio-impédancémétrie est une technique de mesure non invasive du débit cardiaque facile à effectuer en préopératoire. Les renseignements fournis et en particulier les indices de remplissage pourraient être une aide à la décision d'investigations complémentaires pour les cas de risque intermédiaire.
Non-Invasive Measurement of Cardiac Contractility, Stroke Volume and Cardiac Output

ASA, October 17-21, 2009, New Orleans, LA

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Introduction:
The Electrical-Mechanical Interval is the time between a specific event on ECG, and its corresponding mechanical event in a peripheral artery. Let \( E \) be the instant when the ECG voltage, \( ECG(t) \), accelerates maximally upward. \( E \), then, is the time of \( ECG'(t)_{\text{max}} \). Let \( M \) be the instant when the arterial pressure, \( ABP(t) \), accelerates maximally upward. \( M \), then, is the time of \( ABP''(t)_{\text{max}} \). \( ECG''(t) \) and \( ABP''(t) \) are second time derivatives. The time from \( E \) to \( M \), \( (E-M) \), is the 'Electrical Mechanical Interval.' This interval is related to the ratio of the Stroke Volume \( SV \) and Left Ventricular Systolic Ejection Interval \( EI \) by

\[
\text{ln}(SV/EI) = A + B \times \frac{1}{(E-M)}
\]

where \( A \) and \( B \) are empirical constants.

We have previously shown that \( \text{ln}(SV/EI) \) is linearly proportional to \( \text{ln}(dP/dt_{\text{max}}) \) where \( P \) is Left Ventricular Pressure. Hence,

\[
\text{ln}(dP/dt_{\text{max}}) = C + D \times \frac{1}{(E-M)}
\]

where \( C \) and \( D \) are empirical constants. So \( 1/(E-M) \) is also an index of \( dP/dt_{\text{max}} \), or myocardial contractility. The purpose of this study was to demonstrate feasibility of a new method for the non-invasive measurement of myocardial contractility, stroke volume, and cardiac output.

Methods:
After IRB approval a Physioflow® trans-thoracic impedance monitor (Manatec Inc.) was used to measure \( SV \) and \( EI \), in 6 human volunteers. Physioflow® provides an ECG lead II output. A T-line® (Tensys Medical Inc.) was applied over the radial artery. This provided non-invasive \( ABP(t) \). \( (E-M) \) intervals for each heartbeat were calculated using second derivative maxima of ECG and ABP. Subjects were exercised on a stepping machine (Nautilus Inc.) to 80% of maximal heart rate. Data were collected as the heart rate declined from maximum to baseline.

Results:
Corresponding 30-second epochs of \( \text{ln}(SV/EI) \) and \( 1/(E-M) \) data were averaged. We plotted corresponding \( \text{ln}(SV/EI) \) against \( 1/(E-M) \). A calibration curve is shown in fig. 1.

The scaling parameters \( A \) and \( B \) in eq. 1 derived from linear regression of the plotted data were shown to be reproducible with repeated exercise sessions.[figure1]

Conclusion:
Because the T-line and ECG are non-invasive, it is possible, using a device such as Physioflow, to calibrate eq. 1 and determine \( SV/EI \) from \( 1/(E-M) \). Since \( EI \) can be measured non-invasively using Doppler, or impedance measurements, we can determine beat-by-beat \( SV \), and Stroke Volume Variability (SVV). SVV can be used to assess preload in patients having positive-pressure ventilation. Cardiac Output is easily obtained from \( SV/EI*EI/T \) where \( T \) is the period of the cardiac cycle. These results demonstrate feasibility of a novel non-invasive cardiac monitoring technology.
Natural Log of Average Left Ventricular Systolic Volume Outflow Rate

\[ \ln(SV/\Xi) = A + B \times (1/(E-M)) \]

\( A = 4.72662 \)  \( Err = 0.07635 \)
\( B = 0.26989 \)  \( Err = 0.01508 \)
\( R = 0.97019 \)  \( SD = 0.04334 \)
\( N = 22 \)  \( P < 0.0001 \)

\( SV = \) Stroke Volume, cc
\( \Xi = \) Left Ventricular Systolic Ejection Interval, sec

fig. 1
Continuous Cardiac Output Monitoring During Major Intra-Abdominal Surgery: Physioflow Signal-Morphology Impedance Cardiography vs. FloTrac/Vigileo vs. Central Venous Oxygen Saturation

Authors: • Irwin Gratz, D.O., Edward Deal, D.O., Francis Spitz, M.D., Elaine Allen, Ph.D., Erin Pukenas, M.D. Cooper University Hospital, Cooper Medical School at Rowan University, Camden, New Jersey, United States

Abstract: Hemodynamic monitoring and optimizing cardiac output during surgery improves patient outcome [1]. The clinical standard for cardiac output (CO) determination has been thermodilution which requires a pulmonary artery catheter, an invasive procedure with the possibility of numerous complications. Central venous oxygen saturation (ScvO2) has been used as a surrogate for CO monitoring but requires the insertion of a central venous catheter. The risks associated with such catheters have led to advent of the less invasive FloTrac/Vigileo system which estimates CO based on pulse contour analysis from an arterial line. Several new totally non-invasive systems claim ability to accurately display continuous cardiac output values. One such system is the PhysioFlow which determines CO and other parameters based on signal morphology impedance cardiography. The instant changes in thoracic blood volume (a reflection of the stroke volume) cause changes in impedance between the 4 electrodes placed on the neck and thorax. On the basis of these changes in impedance, the computer calculates cardiac output.

The aim of our study was to compare the CO values obtained using Vigileo/FloTrac system with those obtained with the PhysioFlow and correlate both to ScvO2 measurements during major intra-abdominal surgery.

Methods: With IRB approval patients scheduled for major intra-abdominal surgery had simultaneous CO measured using pulse contour analysis by the Vigileo system and PhysioFlow. In addition to central BP, ScvO2 was also monitored during the procedure. Data were combined from the PhysioFlow, Vigileo, ScvO2 and arterial line on a minute by minute basis. Pearson correlation coefficients were calculated between systolic BP and CO by PhysioFlow and Vigileo as well as ScvO2. During periods of electro-cautery, data from the PhysioFlow was not analyzed secondary to interference. Patients were managed aggressively with vasopressors and fluid administration.

Results: CO data from the two devices were plotted over time (see Figure 1). Plots of systolic BP and ScvO2 were overlaid with the same times in the X-axis (see Figure 1). There was virtually no correlation between the Vigileo and PhysioFlow systems (N=239, r² = -0.002, p=0.981). The Vigileo CO values trended well with systolic BP (N=191, r² = 0.730, p<0.001) compared to the PhysioFlow (N=178, r² = 0.081, p=0.280). The PhysioFlow cardiac output values trended better with ScvO2 (N=224, r² = 0.726, p<0.001) compared to the Vigileo (N=252, r² = 0.314, p<0.001).

Conclusion: Cardiac output values obtained with the Vigileo with the 3rd generation software is more variable and appears to mirror changes seen in systolic BP. In contrast, CO values obtained by PhysioFlow are less variable, and trends better with ScvO2. The 3rd-generation FloTrac/Vigileo device appears unreliable for tracking changes in CO during major abdominal surgery.
3 RESEARCH
### 3.1 PHYSIOLOGY

#### Exercise Capacity and Idebenone Intervention in Children and Adolescents with Friedreich Ataxia

*Presented in part to the American College of Sports Medicine, Seattle, WA, May 28, 2009.*

**Authors:**
- Bart E. Drinkard, MSPT, Randall E. Keyser, PhD, Scott M. Paul, MD, Ross Arena, PhD, PT, Jonathan F. Plehn, MD, Jack A. Yanovski, MD, PhD, Nicholas A. Di Prospero, MD, PhD

**Abstract:**

**Objective:**
To determine the exercise capacity of children and adolescents with Friedreich's Ataxia (FA) and to evaluate the effects of 6 months of idebenone treatment on exercise capacity.

**Design:**
Exploratory endpoint in a randomized double-blind, placebo-controlled, phase II clinical trial designed to investigate the effects of idebenone on a biomarker of oxidative stress.

**Setting:**
Exercise physiology laboratory in a single clinical research center.

**Participants:**
Ambulatory subjects (N=48; age range, 9–17y) with genetically confirmed FA.

**Intervention:**
Idebenone administered orally 3 times a day for a total daily dose of approximately 5, 15, and 45mg/kg or matching placebo for 6 months.

**Main Outcome Measures**
Peak oxygen consumption per unit time (peak VO2) and peak work rate (WR) were measured during incremental exercise testing at baseline and after treatment. Echocardiography and neurologic assessments were also completed before and after treatment.

**Results**
Baseline mean peak VO2 ± SD was 746±246mL/min (16.2±5.8mL/kg/min), and WR was 40±23W for all subjects. Peak VO2 and WR were correlated with short guanine-adenine-adenine allele length and neurologic function. Relative left ventricular wall thickness was increased but left ventricular ejection fraction was normal in most subjects; there was no relationship between any exercise and echocardiographic measures. There were no significant changes in mean peak VO2 or WR after idebenone treatment at any dose level relative to placebo.

**Conclusion:**
Exercise capacity in children and adolescents with FA was significantly impaired. The basis for the impairment appears to be multifactorial and correlated to the degree of neurologic impairment. Although idebenone has previously been shown potentially to improve features of FA, idebenone treatment did not increase exercise capacity relative to placebo.
Post Immersion Delayed Vasomotor Adjustments to Dehydration?

European Underwater and Baromedical Society News letter, 2000

Abstract:
While hemodynamic and fluid balance changes have been fairly well studied during immersion, the corresponding changes post-immersion are almost totally ignored. Ten trained divers (33 +/- 5 years) underwent two similar 6 hours hyperbaric hyperoxic exposures with intermittent cycling exercise, one day in dry ambience (DY) and three weeks later immersed up to the neck (IM). They had no food or beverage intake during either session. Whole body weight was assessed and venous blood samples were taken before and 15 min after each exposure session. Venous occlusion of the thighs was performed at 30, 40, 50, 60 mmHg during segmental weighing before and after each session. Segmental weighing performed with our original device allows measuring rapid changes in weight of lower limbs, abdomen-pelvis, and thorax related fluid shifts in the body. The data collected during these manoeuvres provided information about venous tone in the legs through distensibility and compliance assessments, and about arterial flow in the leg and splanchnic vessels. During segmental weighing, stroke volume (SV), cardiac output (CO) and heart rate (HR) were recorded using a Physioflow® impedance cardiography device. As described in a companion paper, on average, the final weight losses were similar in the two ambiences (2.2 kg in DY vs 2.3 kg in IM), whereas plasma contraction was greater in the IM session (-14.7% vs –9.7% in DY; p<0.001) as evidenced by changes. In hematocrite, blood haemoglobin and plasma proteins. Plasma levels of noradrenaline (NA), arginine-vasopressin (APV) were increased 20 min after each session versus pre-exposure, a change 3 times higher after IM than DY (p>0.01). Inversely, atrial and brain natriuretic peptides (ANP and BNP) as well as cyclic guanosine monophosphate (cGMP) remained increased 20 min post IM (p<0.05). Heart rate was decreased after DY (-7 min-1; p<0.05) but slightly increased after IM (+3 min-1; p<0.05). Conversely, stroke volume was more reduced after IM than DY (-9 mL vs –4 mL respectively; p<0.05). Venous compliance and distensibility of the legs were reduced after DY (p<0.05) but preserved after IM. Indexes of arterial flow in both the leg and splanchnic vascular bed were reduced following DY. Thus on the other hand, after DY the increase in plasma vasoconstrictive mediators (NA, APV) likely supported the increased venous and arterial vasomotor tone required to preserve cardiac output and blood pressure, in turn slightly lowering heart rate through baroreflex activation. On the other hand, the paradoxical coexistence of markedly increased levels of NA and APV 30 min post IM together with unchanged vasomotor tone 1) was consistent with the decreased SV and CO but slightly increased HR ; 2) was likely explained by the persistence of high level of natriuretic peptides within the first hour post-immersion.
Cardiovascular and Oxygen Uptake Kinetics during Sequential Heavy Cycling Exercises

Accepted by Canadian Journal of Applied Physiology, May 27, 2002

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Abstract:
The purpose of the present study was to assess the relationship between the rapidity of increased oxygen uptake (VO2) and increased cardiac output (CO) during heavy exercise. Six subjects performed repeated bouts on a cycle ergometer above the ventilatory threshold (~80% of peak VO2) separated by 10-min recovery cycling at 35% peak VO2. VO2 was determined breath-by-breath and CO was determined continuously by impedance cardiography (PhysioFlow, Paris, France). CO and VO2 values were significantly higher during the 2-min period preceding the second bout. The overall responses for VO2 and CO were significantly related, and were faster during the second bout. Prior heavy exercise resulted in a significant increase in the amplitude of the fast component of VO2, with no change in the time constant, and a decrease in the slow component. Under these circumstances, the amplitude of the fast component was more sensitive to prior heavy exercise than was the associated time constant.
3. Research
3.1 Physiology

**Effect of Exercise Intensity on Relationship between VO2max and Cardiac Output**


**Authors:**

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**Abstract:**

Effect of Exercise Intensity on Relationship between VO2max and Cardiac Output.

**Purpose:**

The purpose of this study was to determine whether the maximal oxygen uptake (VO2max) is attained with the same central and peripheral factors according to the exercise intensity.

**Methods:**

Nine well-trained males performed an incremental exercise test on a cycle ergometer to determine the maximal power associated with VO2max (pVO2max) and maximal cardiac output (Qmax). Two days later, they performed two continuous cycling exercises at 100% (tlimΔ100 = 5 min 12 s ± 2 min 25 s) and at an intermediate work rate between the lactate threshold and pVO2max (tlimΔ50 = 12 min 6 s ± 3 min 5 s). Heart rate and stroke volume (SV) were measured (by impedance) continuously during all tests. Cardiac output (Q) and arterial-venous O2 difference (a-vO2 diff) were calculated using standard equations.

**Results:**

Repeated measures ANOVA indicated that: 1) maximal heart rate, VE, blood lactate, and VO2 (VO2max) were not different between the three exercises but Q was lower in tlimΔ50 than in the incremental test (24.4 ± 3.6 L·min⁻¹ vs 28.4 ± 4.1 L·min⁻¹; *P* < 0.05) due to a lower SV (143 ± 27 mL·beat⁻¹ vs 179 ± 34 mL·beat⁻¹; *P* < 0.05), and 2) maximal values of a-vO2 diff were not significantly different between all the exercise protocols but reduced later in tlimΔ50 compared with tlim100 (6 min 58 s ± 4 min 29 s vs 3 min 6 s ± 1 min 3 s, *P* = 0.05). This reduction in a-vO2 diff was correlated with the arterial oxygen desaturation (SaO2 = -15.3 ± 3.9%) in tlimΔ50 (r = -0.74, *P* = 0.05).

**Conclusion:**

VO2max was not attained with the same central and peripheral factors in exhaustive exercises, and tlimΔ50 did not elicit the maximal Q. This might be taken into account if the training aim is to enhance the central factors of VO2max using exercise intensities eliciting VO2max but not necessarily Qmax.
Cardiac Output and Oxygen Release during very High-intensity Exercise Performed until Exhaustion


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Abstract:
Our objectives were firstly, to study the patterns of the cardiac output (Q) and the arteriovenous oxygen difference [(a-v)O2] responses to oxygen uptake (VO2) during constant workload exercise (CWE) performed above the respiratory compensation point (RCP), and secondly, to establish the relationships between their kinetics and the time to exhaustion. Nine subjects performed two tests: a maximal incremental exercise test (IET) to determine the maximal VO2 (VO2peak), and a CWE test to exhaustion, performed at pΔ50 (intermediate power between RCP and VO2 peak). During CWE, VO2 was measured breath-by-breath? Q was measured beat-by-beat with and impedance device, and blood lactate (LA) was sampled each minute. To calculate (a-v)O2, the values of VO2 and Q were synchronised over 10 intervals. A fitting method was used to describe the VO2, Q and (a-v)O2 kinetics. The (a-v) O2 difference followed a rapid monoeponential function, whereas both VO2 and Q were best fitted by a single exponential plus linear increase: the time constant (τ) VO2 [57 (20s) was similar to τ(a-v)O2, whereas τ for Q was significantly higher [89(34)s, P<0.05] (values expressed as the mean and standard error). LA started to increase after 2 min CWE then increased rapidly, reaching a similar maximal value as that seen during the IET. During CWE, the rapid component of VO2 uptake was determined by a rapid and maximal (a-v)O2 extraction coupled with a two-fold longer Q increase. It is likely that lactic acidosis markedly increased oxygen availability, which when associated with the slow linear increase of Q, may account for the VO2 slow component. Time to exhaustion was larger in individuals with shorter time delay for (a-v)O2 and greater τ for Q.

Keywords:
• Oxygen slow component,
• Cardiac Output,
• Arteriovenous oxygen difference,
• Time to exhaustion
Faut-il Mesurer le Débit Cardiaque à L’exercice?

Journées Francophones ALVEOLE, Montpellier, Mars 2004. Dyspnées Cardiologiques Difficiles

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Méthodes:
La mesure du Q à l’effort par impédancémétrie revalorisée par les acquisitions de la technologie moderne (PhysioFlow – Manatec) offre de solides perspectives par rapport aux autres méthodes non invasives (CO₂ rebreathing, échocardiographie, doppler...). Nous l’avons validée par comparaison avec la méthode invasive de Fick au cours de mesures simultanées répétées lors d’une épreuve à puissance constante [3] et lors d’un test d’effort maximal [4] et l’utilisons à présent systématiquement dans nos ECRM. La variation d’impédance produite par la systole permet d’obtenir Q cycle par cycle et de là le VES. En parallèle cette mesure associée à la mesure simultanée de la VO₂ aboutit à une détermination quasi continue de la da v O₂ grâce au calcul du rapport VO₂/Q.

Résultats:
1/ A puissance constante ou lors d’un test maximal à charges croissantes on obtient une détermination directe et quasi continue des ajustements centraux (VES) et périphériques (da v O₂). Nous avons observé ainsi chez les patients des VES d’emblée maximaux ou au contraire s’ajustant jusqu’aux paliers sous maximaux de l’effort. Aucune cinétique évolutive “standard” du VES de l’effort ne peut plus être actuellement affirmée. De même s’agissant de la da v O₂ les valeurs mesurées sont souvent très différentes chez les malades désadaptés que celles communément admises chez les sujets sains, sédentaires ou sportifs.

2/ L’épreuve temps limite : au cours de ce test qui consiste à soutenir à 90% de la VO₂ max du sujet nous pouvons suivre grâce au PhysioFlow la cinétique des grandeurs, Q, FC, VES et, VO₂, da v O₂ et déterminer notamment la constante de temps (τ, τ₀) de chaque monoexponensielle qui les décrit. Chez ces sujets sains la contribution de chaque élément de l’équation de Fick pour assurer à chaque moment l’ajustement de la VO₂ peut être représentée graphiquement – en % de leur valeur maximale. Une telle approche dynamique des ajustements s’avère précieuse chez les cardiaques, tant au plan explicatif que prédicatif : ainsi KOIKE et al ont montré la relation entre les constantes de temps de VO₂ et de Q mesurées lors d’un effort constant et les valeurs des fractions d’éjection ventriculaire gauche mesurées au repos.

Conclusion:
L’origine de toute dyspnée d’effort est certes multifactorielle ; mais chez le cardiaque prédominent le dysfonctionnement myocardique et ses conséquences : la sédentarité, et donc le déconditionnement physique. La mesure continue du débit cardiaque par impédancémétrie (PhysioFlow), associée aux données de l’épreuve cardiorespiratoire, permet de cerner tous les facteurs d’ajustement de la VO₂ tels qu’exprimés dans l’équation de Fick. La généralisation de cette évaluation « intégrative » grâce à une mesure continue et « non invasive » du débit cardiaque devrait ouvrir vers une meilleure compréhension des « dyspnées ». 
### Abstract-Purpose:

Despite identical oxygen uptake (VO2), enhanced heart rate (HR) and cardiac output (Qc) responses have been reported in eccentric (ECC) versus concentric (CON) cycle exercise. The aim of this study was to describe the specific circulatory adjustments (HR and stroke volume (SV)) to incremental ECC cycle exercise in order to: 1) determine the HR values leading to identical VO2 in ECC and CON cycling; and 2) estimate the interindividual variability of this HR correspondence between the two exercise modes, with emphasis upon rehabilitation and training purposes.

### Methods:

Eight healthy male subjects (age, 28 +/- 2 yr) participated in this study. They performed CON and ECC cycle incremental exercises (power output increases of 50 W every 3 min). Breath-by-breath gas exchange analysis and beat-by-beat thoracic impedancemetry were used to determine VO2 and Qc, respectively.

### Results:

At the same metabolic power VO2 of 1.08 +/- 0.05 L/min in CON vs 1.04 +/- 0.06 L/min in ECC, SV was not different, but HR was 17% higher in ECC (P < 0.01), leading to a 27% enhanced Qc (P < 0.01). Qc and HR net adjustments (exercise minus resting values) in ECC versus CON muscle involvement demonstrated important interindividual variability with coefficients of variation amounting to 32% and 30%, respectively.

### Conclusion:

In practice, if a given level of VO2 is to be reached, ECC HR has to be set above the CON one. Taking into account the interindividual variability of the circulatory adjustments in ECC versus CON muscle involvement, a precise HR correspondence can be established individually from the VO2/HR relationship obtained using ECC incremental testing, allowing prescription of accurate target HR for rehabilitation or training purposes.

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3. Research

3.1 Physiology

Heart Rate Deflection Point as a Strategy to Defend Stroke Volume during Incremental Exercise


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**Abstract:**

The purpose of this study was to examine whether the heart rate (HR) deflection point (HRDP) in the HR-power relationship is concomitant with the maximal stroke volume (SV_max) value achievement in endurance-trained subjects. Twenty-two international male cyclists (30.3 ± 7.3 yr, 179.7 ± 7.2 cm, 71.3 ± 5.5 kg) undertook a graded cycling exercise (50 W every 3 min) in the upright position. Thoracic impedance was used to measure continuously the HR and stroke volume (SV) values. The HRDP was estimated by the third-order curvilinear regression method. As a result, 72.7% of the subjects (HRDP group, n = 16) presented a break point in their HR-work rate curve at 89.9 ± 2.8% of their maximal HR value. The SV value increased until 78.0 ± 9.3% of the power associated with maximal O2 uptake (VO2_max) in the HRDP group, whereas it increased until 94.4 ± 8.6% of the power associated with VO2_max in six other subjects (no-HRDP group, P = 0.004). Neither SV_max (ml/beat or ml·beat−1·m−2) nor VO2_max (ml/min or ml·kg−1·min−1) were different between both groups. However, SV significantly decreased before exhaustion in the HRDP group (153 ± 44 vs. 144 ± 40 ml/beat, P = 0.005). In the HRDP group, 62% of the variance in the power associated with the SV_max could also be predicted by the power output at which HRDP appeared. In conclusion, in well-trained subjects, the power associated with the SV_max-HRDP relationship supposed that the HR deflection coincided with the optimal cardiac work for which SV_max was attained.

**Keywords:**

- Physical work curve break point,
- Left ventricular ejection fraction,
- Cycling graded test
Evolution of Cardiac Output during Resistive Exercise in the Healthy Subject

Presented at the CSEP conference, Quebec, 2005

Abstract:
Muscular reinforcement is a type of training that is often used in physical rehabilitation. The acute impact of such training on cardiac training is not well known. It seems important to understand this hemodynamic response better in order to apply this technique to numerous different patient populations, including cardiac patients. The aim of this study is to follow the evolution of cardiac parameters (heart rate (HR), blood pressure (SBP and DBP), cardiac output (Qc), stroke volume (SV), and derivative parameters (rate pressure product RPP, and peripheral systemic resistance PSR) in a continuous and non-invasive manner during a classical resistive training.

Methods
23 healthy subjects (average age: 24 years) realised 3 series of 10 knee flexion-extensions on a quadriceps chair (Technogym). The imposed load was 75% of maximal voluntary contraction (MVC). The work rhythm was of 1 second for a complete extension and 1 second to return to the flexed position. The recovery period was fixed at 1 minute between series. The blood pressure was continuously measured with the "Finapres". Qc and SV were continuously measured with a "Physio-flow".

Results:
We observe an 8 to 36 % increase of Qc during the exercise. The Qc decreases during the periods of rest but never reaches the starting values within the imposed 1 minute of rest time. This increase of Qc is essentially due to an increase of the HR (+ 45, 19 and 11% during the first, second and third series). The SV practically doesn't vary (+/- 5%). The observed raise of Qc is relatively low compared to what is described in the literature for an equivalent dynamic effort (75% of VO2 max / 75 %CMV). The DP follows an evolution previously described in the literature.

Conclusion:
The Qc increases in a moderate manner during a short but intense resistive effort. The Qc doesn’t return to the rest values within 1 minute of recovery. The SV contributes little to the raise of Qc. The raise of Qc is essentially due to the HR increase.
Non-invasive Evaluation of Maximal Arteriovenous Oxygen Difference and Adolescent Boys’ Fitness Levels

Objective:
To evaluate non-invasively the patterns of the Fick equation components during an incremental ergocycle test.

Methods:
Simultaneous measurements of gas exchanges and cardiac output \( \dot{Q_c} \) — thoracic impedance device Physioflow Manatec — supply the Fick equation's variables:
\[
\dot{V}O_2 = \dot{Q_c} \times d(a - \bar{v})O_2.
\]
Their dynamics are studied at 1st and 2nd ventilatory threshold (SV1, SV2) and at PMT (Max Tolerated Power) in 41 active adolescent boys; 25 of them are highly trained (TP) and 16 occasionally (P). There is no anthropometric difference between the 2 groups.

Results:
1) Individual slopes "a" of \( \dot{Q_c} \) regression against \( \dot{V}O_2 \) are negative: the higher the "a" value the lower \( \dot{V}O_2 \text{max} \), PMT, maximal tissular \( O_2 \) extraction \( d(a - \bar{v})O_2 \text{max} \), and the adolescents' performance;
2) as early as at SV1, \( d(a - \bar{v})O_2 \text{ln TP} \) is always higher than in P; whereas \( \dot{Q_c} \), FC and stroke volume (VES) have similar values in both groups at SV1, SV2 and PMT; 3) in all subjects, TP and P, VES max and \( d(a - \bar{v})O_2 \text{max} \) were reached at the level of SV2.

Conclusion:
Non-invasive and simultaneous \( \dot{Q_c} \) and \( \dot{V}O_2 \) measurements during incremental test lead to Fick equation adjustments, \( \dot{Q_c} / \dot{V}O_2 \) a" slope and \( d(a - \bar{v})O_2 \) difference contributing thus to interesting indications of subjects’ fitness.
Children Cardiorespiratory Performance Index by Simultaneous and Independent Measure of Oxygen Uptake and Cardiac Output

Science & Sports Volume 22, Issue 2, April 2007, Pages 120-122

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Objective:
To demonstrate that the linear coefficient of the \( \frac{\dot{Q}c}{\dot{V}o_2} \) relationship is an indice of the tissular oxygen extraction capacity \( d (a - \bar{v})o_2 \) in children.

Keywords:
• Non-invasive cardiac output
• \( O_2 \) arteriovenous difference
• PhysioFlow slope analysis

Synthesis of facts:
Twelve soccers (11.7 ± 0.7 years) performed a maximal progressive test. Our results show that \( \dot{Q}c \) is strongly correlated with \( \dot{V}o_2 (r = 0.96, p < 0.01) \), and the individual values of the linear coefficient of the \( \dot{Q}c - \dot{V}o_2 \) relationship are conversely correlated with \( d (a - \bar{v})o_2 \max \) values \( (r = -0.91, p < 0.05) \).

Conclusion:
It thus seems that \( d (a - \bar{v})o_2 \max \) is the main predicting factor for \( \dot{V}o_2 \max \).
Effect of Interval versus Continuous Training on Cardiorespiratory and Mitochondrial Functions: Relationship to Aerobic Performance Improvements in Sedentary

Am J Physiol Regul Integr Comp Physiol, 2008 Apr 16.

Authors:

Abstract:
The goal of the study was to determine the effects of continuous (CT) vs. intermittent (IT) training yielding identical mechanical work and training duration on skeletal muscle and cardiorespiratory adaptations in sedentary subjects. Eleven subjects (6 men and 5 women, 45+/-3 years) were randomly assigned to two periods of 24 trainings sessions over 8 weeks in a cross-over design, separated by 12 weeks of detraining. Maximal oxygen uptake (VO2max) measured during maximal exercise testing increased after both trainings (9% with CT vs. 15% with IT), whereas only IT was associated with faster VO2 kinetics (tau: 68.0+/-1.6 vs. 54.9+/-0.7 sec, p<0.05) measured during a test to exhaustion (TTE) and with improvements in maximal cardiac output (Qmax, from 18.1+/-1.1 to 20.1+/-1.2 L.min(-1), p<0.01). Skeletal muscle mitochondrial oxidative capacities (Vmax) were only increased after IT (3.3+/-0.4 before and 4.5+/-0.6 micromol O2.min(-1).gdw(-1) after training, p<0.05) whereas capillary density increased after both trainings, with a 2-fold higher enhancement after CT (+21+/-1% for IT and +40+/-3% after CT, p<0.05). The gain of Vmax was correlated with the gain of TTE and the gain of VO2max with IT. The Gain of Qmax was also correlated with the gain of VO2max. These results suggest that fluctuations of workload and oxygen uptake during training sessions, rather than exercise duration or global energy expenditure, are key factor in improving muscle oxidative capacities. In an integrative view, IT seems optimal in maximizing peripheral muscle and central cardiorespiratory adaptations, permitting significant functional improvement. These data support the symmorphosis concept in sedentary subjects. Key words: mitochondria, endurance training, performance.
Shock and Awe: Hemodynamic Changes during ECT Measured with a Non-Invasive Cardiac Output Monitor

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October 15, 2006
2:00 PM - 4:00 PM
Room Hall E, Area G

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Introduction:
Typical cardiovascular effects of ECT include hypertension and tachycardia. Blood pressure tends to transiently increase 30-40% and there is about a 10% increase in heart rate (1). These changes result from an increase in sympathetic nervous system activity following an initial parasympathetic response to a seizure. There is little information about the hemodynamic changes occurring in patients with normal cardiac function during this procedure.
We investigated the changes occurring in normal subjects using a thoracic bioimpedance monitor to assess cardiac function.

Methods:
Patients were enrolled in the study after providing informed consent. Patients with cardiovascular disease were excluded from this study. General anesthesia was induced with glycopyrrolate, 0.1-0.2 mg; propofol, 1-1.5 mg/kg; and succinylcholine, 1 mg/kg. Patients were ventilated by mask with 100% oxygen throughout the treatment. Continuous hemodynamic measurements were made using a PhysioFlow™ thoracic bioimpedance cardiac output monitor. Patients were followed throughout their treatment with measurements recorded at the following intervals: baseline, immediately pre-seizure stimulus, 1 min after end of seizure stimulus and 5 min after end of seizure stimulus. The data was analyzed using the student's t-test for paired samples.

Results:
Nine patients (M:F=2/5), were studied. The average age was 39.7 ± 9.5 yrs (range: 23-52 yr). Eleven treatments in were studied in total. The BSA was 1.91 ± 0.31 (range:1.31-2.02). The CI gradually decrease through to 1 min after the end of seizure stimulus and then increases. The HR and SV were constant through the treatment period. There is a trend of increasing EDV with decreasing EF and systemic vascular resistance during the treatment and into the post-ictal phase.

Conclusion:
The CI is maintained during ECT and increases in the post-ictal period. The EDV gradually increases while the EF decreases, resulting in a rather constant SV throughout the treatment. Because there is a trend toward decreasing SVR and since no intravenous fluids were administered during these treatments, the increase in EDV probably reflects transient cardiovascular depression from propofol. These observations reflect how younger patients without cardiovascular disease respond to propofol anesthesia and the stress of ECT. The changes are consistent with other reports in the literature suggesting that non-invasive hemodynamic monitoring is reliable in clinical situations. Evaluation of the hemodynamic response in older patients (>65 yr) without cardiovascular disease is in progress.

Abstract:
Aerobic performance is dependent on both cardio-respiratory and peripheral factors with hemodynamic parameters playing a major role. However, whether blood rheology might affect aerobic performance through an effect on hemodynamic factors is not known. The aim of the present study was to assess the relationships between hemodynamic, hemorheological and metabolic parameters in response to a sub-maximal cycling exercise protocol consisting of three successive levels of nine min duration (50, 100 and 150 W). Ten young sportsmen participated in the present study. Mean arterial pressure (MAP) was measured manually, with thoracic impedance used to monitor cardiac output (Qc); systemic vascular resistance (SVR) was then calculated. Whole blood viscosity (ηb) was measured and used to calculate systemic vascular hindrance. Hematocrit (Hct) was determined by microcentrifugation and red blood cell (RBC) deformability (EI) was determined by ectactometry. A breath-by-breath gas analyzer was used to measure oxygen uptake (VO2); the Fick equation was used to calculate arteriovenous oxygen difference [(a-v)O2] from VO2 and Qc. All measurements were performed at rest, during exercise and during recovery. Compared to baseline, Qc, MAP, Hct, EI, VO2, and (a-v)O2 increased during exercise. ηb increased above baseline only at 150 W and remained elevated during recovery; the increase in ηb during the last level of exercise was associated with a decrease of SVR and systemic vascular hindrance. There was a significant negative correlation between EI and SVR \((r = -0.35, p < 0.01)\) and a significant positive relationship between EI and (a-v)O2 \((r = 0.35, p < 0.01)\) and between EI and VO2 \((r = 0.37, p < 0.01)\) across all exercise workloads, thus suggesting a potential role for RBC deformability as a factor affecting aerobic performance via oxygen delivery to tissues. These data lend support to the concept that hemorheological parameters may contribute to hemodynamic and cardio-respiratory adaptations in response to exercise in moderately trained sportsmen.

Keywords:
- Blood rheology,
- Exercise physiology,
- Hemodynamics,
- Oxygen uptake
Oxygen uptake efficiency slope’ in trained and untrained subjects exposed to hypoxia


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Accepted 26 January 2008

**Abstract:**
We assessed the ability of the oxygen uptake efficiency slope, whether calculated on 100 and 80% of maximal exercise test duration (OUES100 and OUES80), to identify the change in cardiorespiratory capacities in response to hypoxia in subjects with a broad range of VO2 peak. Four maximal exercise tests were performed in trained (T) and untrained subjects (UT) in normoxia and at 1000, 2500 and 4500 m. The mean reductions in maximal exercise capacities at 4500m were the same in T subjects for VO2 peak (−30%), OUES80 (−26%) and OUES100 (−26%) whereas in UT subjects only OUES100 (−14%), but not OUES80 (−20%), was lower compared with VO2 peak (−21%, p < 0.05). OUES100 and OUES80 were correlated with VO2 peak and the ventilatory anaerobic threshold in both groups. Multiple regression analyses showed that VO2 peak, OUES100 and OUES80 were significantly linked to O2 arterial-venous difference. The OUES80 could be considered as an interesting sub-maximal index of cardiorespiratory fitness in normal or hypoxemic subjects unable to reach VO2 peak.

**Keywords:**
- Hypoxia;
- Exercise;
- Ventilatory response;
- Testing;
- OUES;
- O2 utilisation;
- Fitness;
- Training

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Determinant factors of the decrease in aerobic performance in moderate acute hypoxia in women endurance athletes


Abstract:
The purpose of this study was to evaluate the limiting factors of maximal aerobic performance in endurance trained (TW) and sedentary (UW) women. Subjects performed four incremental tests on a cycle ergometer at sea level and in normobaric hypoxia corresponding to 1000, 2500 and 4500 m. Maximal oxygen uptake decrement ($\Delta VO_2 max$) was larger in TW at each altitude. Maximal heart rate and ventilation decreased at 4500m in TW. Maximal cardiac output remained unchanged. In both groups, arterialized oxygen saturation (SaO2 max) decreased at and above 2500m and maximal O2 transport (QaO2 max) decreased from 1000m. At 4500m, there was no more difference in QaO2 max between TW and UW. Mixed venous O2 pressure (PvO2 max) was lower and O2 extraction (O2ER max) greater in TW at each altitude. The primary determinant factor of VO2 max decrement in moderate acute hypoxia in trained and untrained women is a reduced maximal O2 transport that cannot be compensate by tissue O2 extraction.

Keywords:
• Cardiac output;
• Arterial O2 saturation;
• Venous O2 saturation;
• Tissue O2 extraction
Determinants of maximal oxygen uptake in moderate acute hypoxia in endurance athletes

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Abstract:
The factors determining maximal oxygen consumption were explored in eight endurance trained subjects (TS) and eight untrained subjects (US) exposed to moderate acute normobaric hypoxia. Subjects performed maximal incremental tests at sea level and simulated altitudes (1,000, 2,500, 4,500 m). Heart rate (HR), stroke volume (SV), cardiac output (Q) arterialized oxygen saturation (Sa’O₂), oxygen uptake (VO₂max), ventilation (VE; expressed in normobaric conditions) were measured. At maximal exercise, ventilatory equivalent (VE/VO₂max), O₂ transport (QaO₂max) and O₂ extraction (O₂ERmax) were calculated. In TS, Qmax remained unchanged despite a significant reduction in HRmax at 4,500 m. SVmax remained unchanged. VEmax decreased in TS at 4,500 m, VE/VO₂max was lower in TS and greater at 4,500 m vs. sea level in both groups. Sa’O₂max decreased at and above 1,000 m in TS and 2,500 m in US, O₂ERmax increased at 4,500 m in both groups. QaO₂max decreased with altitude and was greater in TS than US up to 2,500 m but not at 4,500 m. VO₂max decreased with altitude but the decrement (ΔVO₂max) was larger in TS at 4,500 m. In both groups ΔVO₂max in moderate hypoxia was correlated with ΔQaO₂max. Several differences between the two groups are probably responsible for the greater ΔVO₂max in TS at 4,500 m: (1) the relative hypoventilation in TS as shown by the decrement in Vₑmax at 4,500 m (2) the greater QaO₂max decrement in TS due to a lower Sa’O₂max and unchanged Qmax, 3) the smaller increase in O₂ERmax in TS, insufficient to compensate the decrease in Q₄O₂max.

Keywords:
• Aerobic performance;
• Cardiac output;
• Arterial O2 saturation;
• Venous O2 saturation;
• Tissue O2 extraction
Improvement of VO2 max by cardiac output and oxygen extraction adaptation during intermittent versus continuous endurance training


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Abstract:
Improvement of exercise capacity by continuous (CT) versus interval training (IT) remains debated. We tested the hypothesis that CT and IT might improve peripheral and/or central adaptations, respectively, by randomly assigning 10 healthy subjects to two periods of 24 trainings sessions over 8 weeks in a cross-over design, separated by 12 weeks of detraining. Maximal oxygen uptake (VO$_{2\max}$); cardiac output (Q$_{\max}$) and maximal arteriovenous oxygen difference (D$_{a-v}$O$_{2\ max}$) were obtained during an exhaustive incremental test before and after each training period. VO$_{2\max}$ and Q$_{\max}$ increased only after IT (from 26.3 ± 1.6 to 35.2 ± 3.8 ml min$^{-1}$ kg$^{-1}$ and from 17.5 ± 1.3 to 19.5 ± 1.8 l min$^{-1}$, respectively; P < 0.01). D$_{a-v}$O$_{2\ max}$ increased after both protocols (from 11.0 ± 0.8 to 12.7 ± 1.0; P < 0.01 and from 11.0 ± 0.8 to 12.1 ± 1.0 ml 100 ml$^{-1}$, P < 0.05 in CT and IT, respectively). At submaximal intensity a significant rightward shift of the Q/D$_{a-v}$O2 relationship appeared only after CT. These results suggest that in isoenergetic training, central and peripheral adaptations in oxygen transport and utilization are training-modality dependant. IT improves both central and peripheral components of VO$_{2\ max}$ whereas CT is mainly associated with greater oxygen extraction.

Keywords:
• Training modality
• Cardiac output,
• Arteriovenous difference,
• Maximal oxygen consumption,
• Sedentary subjects
Vasoconstrictive Response in the Vascular Beds of the Non-Exercising Forearm During Leg Exercise in Patients With Mild Chronic Heart Failure

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Background:
Reduced exercise capacity may be related to decreased redistribution of blood flow from the nonexercising tissues to the exercising skeletal muscle in patients with mild chronic heart failure (CHF).

Keywords:
• Blood flow;
• Exercise;
• Forearm;
• Heart failure;
• Oxygen consumption

Methods & Results:
In the present study 14 patients with mild CHF and 10 healthy subjects (N) underwent symptom-limited multistage-ergometer exercise, during which forearm vascular resistance (FVR), cardiac index (CI), systemic vascular resistance index (SVRI), and oxygen uptake (VO2) were measured non-invasively using the plethysmograph, impedance, and respiratory gas analysis methods, respectively. The VO2 and CI at peak exercise were lower (p<0.01 each), and SVRI and FVR at both rest and peak exercise were higher in the CHF group than in N. However, both the percent increase in FVR and percent decrease in SVRI from the resting state to peak exercise were lower in CHF than N, and both of them correlated with not only peak VO2, but also the corresponding resting value of FVR and SVRI (p<0.01 each).

Conclusion:
Redistribution of blood flow from the non-exercising tissues to the working skeletal muscles, which may participate in exercise capacity, can be blunted in CHF. The decreased vasoconstrictive response in the non-exercising tissues is intimately related to the increased resting vascular tone in CHF. (Circ J 2007; 71: 922 – 928)
Expiratory muscle loading increases intercostal muscle blood flow during leg exercise in healthy humans

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Abstract:

We investigated whether expiratory muscle loading induced by the application of expiratory flow limitation (EFL) during exercise in healthy subjects causes a reduction in quadriceps muscle blood flow in favour of the blood flow to the intercostal muscles. We hypothesized that during exercise with EFL quadriceps muscle blood flow would be reduced, whereas intercostal muscle blood flow would be increased compared to exercise without EFL. We initially performed an incremental exercise test on eight healthy male subjects with a Starling resistor in the expiratory line limiting expiratory flow to ~ 1 L/sec-1 to determine peak EFL exercise workload (WRpeakEFL). On a different day, two constant-load exercise trials were performed in a balanced ordering sequence during which subjects exercised with or without EFL at WRpeakEFL for 6 minutes. Intercostal (probe over the 7th intercostal space) and vastus lateralis muscle blood flow index (BFI) was calculated by near-infrared spectroscopy using indocyanine green, whereas cardiac output (CO) was measured by an impedance cardiography technique. At exercise termination CO and stroke volume (SV) were not significantly different during exercise with or without EFL (CO: 16.5 vs 15.2 l/min-1, SV: 104 vs 107 ml/beat-1, respectively). Quadriceps muscle BFI during exercise with EFL (5.4 nM/s) was significantly (p = 0.043) lower compared to exercise without EFL (7.6 nM/s), whereas intercostal muscle BFI during exercise with EFL (3.5 nM/s) was significantly (p = 0.021) greater compared to that recorded during control exercise (0.4 nM/s). In conclusion, increased respiratory muscle loading during exercise in healthy humans causes an increase in blood flow to the intercostal muscles and a concomitant decrease in quadriceps muscle blood flow.

Keywords:

• Exercise;
• Expiratory flow limitation;
• Intercostal muscle blood flow;
• Quadriceps muscle blood flow.
Cardiac function and arteriovenous oxygen difference during exercise in obese adults

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• Raul Y. Zubia

Abstract:
The purpose of this study was to assess cardiac function and arteriovenous oxygen difference (a-vO2difference) at rest and during exercise in young, normal-weight (n = 20), and obese (n = 12) men and women who were matched for age and fitness level. Participants were assessed for body composition, peak oxygen consumption (VO2peak), and cardiac variables (thoracic bioimpedance)—cardiac index (CI), cardiac output (Q), stroke volume (SV), heart rate (HR), and ejection fraction (EF)—at rest and during cycling exercise at 65% of VO2peak. Differences between groups were assessed with multivariate ANOVA and mixed-model ANOVA with repeated measures controlling for sex. Absolute VO2peak and VO2peak relative to fat-free mass (FFM) were similar between normal-weight and obese groups (Mean ± SEE 2.7 ± 0.2 vs. 3.3 ± 0.3 l min−1, p = 0.084 and 52.4 ± 1.5 vs. 50.9 ± 2.3 ml kg FFM−1 min−1, p = 0.583, respectively). In the obese group, resting Q and SV were higher (6.7 ± 0.4 vs. 4.9 ± 0.1 l min−1, p < 0.001 and 86.8 ± 4.3 vs. 65.8 ± 1.9 ml min−1, p < 0.001, respectively) and EF lower (56.4 ± 2.2 vs. 65.5 ± 2.2%, p = 0.003, respectively) when compared with the normal-weight group. During submaximal exercise, the obese group demonstrated higher mean CI (8.8 ± 0.3 vs. 7.7 ± 0.2 l min−1 m−2, p = 0.007, respectively), Q (19.2 ± 0.9 vs. 13.1 ± 0.3 l min−1, p < 0.001, respectively), and SV (123.0 ± 5.6 vs. 88.9 ± 4.1 ml min−1, p < 0.001, respectively) and a lower a-vO2 difference (10.4 ± 1.0 vs. 14.0 ± 0.7 ml 100 ml−1, p = 0.002, respectively) compared with controls. Our study suggests that the ability to extract oxygen during exercise may be impaired in obese individuals.

Keywords:
• Cardiac function
• Exercise
• Obese
• Stroke volume
Effects of Acute Hypoxia at Moderate Altitude on Stroke Volume and Cardiac Output During Exercise

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*Vol. 51 (2010), No. 3 pp.170-175*

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**Abstract:**
It has been unclear how acute hypoxia at moderate altitude affects stroke volume (SV), an index of cardiac function, during exercise. The present study was conducted to reveal whether acute normobaric hypoxia might alter SV during exercise.

Nine healthy male subjects performed maximal exercise testing under normobaric normoxic, and normobaric hypoxic conditions (O₂: 14.4%) in a randomized order. A novel thoracic impedance method was used to continuously measure SV and cardiac output (CO) during exercise.

Acute hypoxia decreased maximal work rate (hypoxia; 247 ± 6 [SE] versus normoxia; 267 ± 8 W, (P < 0.005) and VO₂ max (hypoxia; 2761 ± 99 versus normoxia; 3039 ± 133 mL/min, P < 0.005). Under hypoxic conditions, SV and CO at maximal exercise decreased (SV: hypoxia; 145 ± 11 versus normoxia; 163 ± 11 mL, P < 0.05, CO: hypoxia; 26.7 ± 2.1 versus normoxia; 30.2 ± 1.8 L/min, P < 0.05). In acute hypoxia, SV during submaximal exercise at identical work rate decreased. Furthermore, in hypoxia, 4 of 9 subjects attained their highest SV at maximal exercise, while in normoxia, 8 of 9 subjects did.

Acute normobaric hypoxia attenuated the increment of SV and CO during exercise, and SV reached a plateau earlier under hypoxia than in normoxia. Cardiac function during exercise at this level of acute normobaric hypoxia might be attenuated. (Int heart J 2010 : 170-175)

**Keywords:**
- Normobaric hypoxia
- Cardiac output
- Oxygen uptake
- Exercise testing
Maximal exercise limitation in functionally overreached triathletes: role of cardiac adrenergic stimulation.


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**Background:**

Functional overreaching (F-OR) induced by heavy load endurance training programs has been associated with reduced heart rate values both at rest and during exercise. Because this phenomenon may reflect an impairment of cardiac response, this research was conducted to test this hypothesis.

**Keywords:**

• Cardiac response
• Endurance training
• Fatigue
• Overreaching
• Overtraining

**Methods & Results:**

Thirty-five experienced male triathletes were tested (11 control and 24 overload subjects) before overloading (Pre), immediately after overloading (Mid) and after a 2-week taper period (Post). Physiological responses were assessed during an incremental cycling protocol to volitional exhaustion, including catecholamine release, oxygen uptake (VO₂), arteriovenous O₂ difference, cardiac output (Q), systolic (SBP) and diastolic blood pressure (DBP). Twelve subjects of the overload group developed signs of F-OR at Mid (decreased performance with concomitant high perceived fatigue), while 12 others did not (acute fatigue group, AF). VO₂max was reduced only in F-OR subjects at Mid. Lower Q and SBP values with greater arteriovenous O₂ difference were reported in F-OR subjects at all exercising intensities, while no significant change was observed in the control and AF groups. A concomitant decrease in epinephrine excretion was reported only in the F-OR group. All values returned to baseline at Post.

**Conclusion:**

Following an overload endurance training program leading to F-OR, the cardiac response to exhaustive exercise is transiently impaired, possibly due to reduced epinephrine excretion. This finding is likely to explain the complex process of underperformance syndrome experienced by F-OR endurance athletes during heavy load programs.
Cardiovascular and hemodynamic responses on dryland vs. immersed cycling

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Article history: Received 9 June 2014 Received in revised form 29 July 2014 Accepted 13 August 2014

Objectives:
To investigate the effect of water immersion on oxygen uptake (\(\dot{V}O_2\)) and central hemodynamic responses during incremental maximal exercise at the same external power output (\(P_{\text{ext}}\)) and recovery on an immersible ergocycle vs. a dryland ergocycle.

Methods:
Twenty healthy participants (32 ± 7 years; 173 ± 6 cm; 71.7 ± 9.7 kg) performed maximal incremental exercise tests while pedalling either immersed on immersible ergocycle (Hydrorider\textsuperscript{\textregistered}) or on dryland ergocycle (Ergoline 800S; Bitz, Germany). Initial \(P_{\text{ext}}\) of dryland ergocycle protocol was set at 25 W and increased by 25 W every minute until exhaustion. \(P_{\text{ext}}\) on immersible ergocycle was controlled by pedalling rate (rpm). Initial rpm was set at 40 rpm and was increased by 10 rpm until 70 rpm and thereafter by 5 rpm until exhaustion. Gas exchange and central hemodynamic parameters were measured continuously during exercise and a 5-min recovery period. Reported \(\dot{V}O_2\), stroke volume, cardiac output (\(\dot{Q}\)) and arteriovenous difference (\(C(a-v)O_2\)) were compared.

Conclusion:
During exercise and recovery in immersion, \(\dot{V}O_2\) and \(C(a-v)O_2\) were reduced in healthy young participants. We may believe that the reduced muscle \(O_2\) extraction during immersion could occur due to increased blood flow and hyper perfusion of lower limb skeletal muscle, reducing red cell transit time and thereby decreasing muscle oxygen diffusion. In parallel, during immersed cycling exercise, stroke volume and cardiac output were improved for the same \(P_{\text{ext}}\). This may be due to a combination of decreased afterload and/or increased contractility. During recovery, immersion increased stroke volume, ejection fraction and contractility presumably via an increased sensitivity of cardiac contractile proteins to calcium. Further studies are needed to understand by which mechanisms \(\dot{V}O_2\) is decreased during water exercise on IE at the same external power output (\(P_{\text{ext}}\)) relative to exercise on DE.
3. Research
3.1 Physiology

Effect of interval training on cognitive functioning and cerebral oxygenation in obese patients: a pilot study

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Objectives:
To assess the effect of a 4-month high-intensity interval training programme on cognitive functioning, cerebral oxygenation, central haemodynamic and cardiometabolic parameters and aerobic capacity in obese patients.

Methods:
Cognitive functioning, cerebral oxygenation, central haemodynamic, cardiometabolic and exercise parameters were measured before and after a 4-month high-intensity interval training programme in 6 obese patients (mean age 49 years (standard deviation 8), fat mass percentage 31 ± 7%).

Results:
Body composition (body mass, total and trunk fat mass, waist circumference) and fasting insulin were improved after the programme (p < 0.05). VO₂ and power output at ventilatory threshold and peak power output were improved after the programme (p < 0.05). Cognitive functioning, including short-term and verbal memory, attention and processing speed, was significantly improved after training (p < 0.05). Cerebral oxygen extraction was also improved after training (p < 0.05).

Conclusion:
These preliminary results indicate that a 4-month high-intensity interval training programme in obese patients improved both cognitive functioning and cerebral oxygen extraction, in association with improved exercise capacity and body composition.

IMPORTANT NOTE FROM THE MANUFACTURER:
It is likely that the use of stroke volume index and cardiac index in lieu of stroke volume and cardiac output would have shown bigger changes thanks to the training-related weight loss. Normalizing SV et CO with the lean body mass could have been an interesting avenue as well.
Reproducibility of cardiac output derived by impedance cardiography during postural changes and exercise

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Background:
Evaluation of cardiac output (CO) and other haemodynamic parameters may aid in understanding factors involved in arterial blood pressure (BP) changes with exercise and postural stress. Impedance cardiography offers a rapid, non-invasive means to acquire this information, however there is limited data assessing the reproducibility of this technique during haemodynamic perturbation. This study aimed to assess reproducibility of CO and other haemodynamic parameters derived from impedance cardiography during exercise and in different postures.

Methods:
51 participants (mean age 57 _ 9 years, 57% male) had CO and other haemodynamic variables (including end diastolic volume, left ventricular work, ejection fraction and systemic vascular resistance) measured via impedance cardiography (Physio Flow) at two visits separated by 12 _ 7 days. Measures were recorded at rest in three postures (supine, seated and standing), during upright cycle ergometry at a fixed workload (40 W), and also during steady state exercise at an intensity of 60% and 70% of age-predicted maximum heart rate (HR_max).

Results
CO reproducibility was assessed over a wide range (5.27 _ 1.00e12.09 _ 2.02 l/min). There was good agreement between CO measured at each visit in all postures and exercise conditions (intra-class correlation coefficient [ICC] range 0.729e0.888, P < 0.05 for all) with a small difference between visits (mean difference 0.06 _ 1.10 l/min). All other haemodynamic variables showed good agreement between visits (ICC range 0.714e0.970, P < 0.05 for all).

Conclusion:
Non-invasive impedance cardiography provides an acceptably reproducible means to evaluate CO and other haemodynamic variables relevant to arterial BP regulation during different postures and light-to-moderate intensity exercise.

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Increased cardiac output elicits higher VO_{2\text{max}} in response to self-paced exercise

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Abstract:
Recently, a self-paced protocol demonstrated higher energy (maximal oxygen uptake) versus the traditional ramp protocol. The primary aim of the current study was to further explore potential differences in maximal oxygen uptake between the ramp and self-paced protocols using simultaneous measurement of cardiac output. Active men and women of various fitness levels (N = 30, mean age = 26.0 ± 5.0 years) completed 3 graded exercise tests separated by a minimum of 48 h. Participants initially completed progressive ramp exercise to exhaustion to determine maximal oxygen uptake followed by a verification test to confirm maximal oxygen uptake attainment. Over the next 2 sessions, they performed a self-paced and an additional ramp protocol. During exercise, gas exchange data were obtained using indirect calorimetry, and thoracic impedance was utilized to estimate hemodynamic function (stroke volume and cardiac output). One-way ANOVA with repeated measures was used to determine differences in maximal oxygen uptake and cardiac output between ramp and self-paced testing. Results demonstrated lower (p < 0.001) maximal oxygen uptake via the ramp (47.2 ± 10.2 mL · kg\(^{-1}\) · min\(^{-1}\)) versus the self-paced (50.2 ± 9.6 mL · kg\(^{-1}\) · min\(^{-1}\)) protocol, with no interaction (p = 0.06) seen for fitness level. Maximal heart rate and cardiac output (p = 0.02) were higher in the self-paced protocol versus ramp exercise. In conclusion, data show that the traditional ramp protocol may underestimate maximal oxygen uptake compared with a newly developed self-paced protocol, with a greater cardiac output potentially responsible for this outcome.

Keywords: maximal oxygen uptake, stroke volume, cycle ergometer, RPE, VO_{2\text{max}} limitations

Results:
With the exception of 1 male in HIGH who did not complete his final RAMP test because of an acute injury, all participants completed all trials during the study. Data were combined for men and women across groups, as no significant sex interaction (p > 0.05) was revealed.

Conclusion:
In 30 men and women differing in fitness levels, a self-paced cycling protocol demonstrated higher VO_{2\text{max}} than the traditional RAMP, which was consequent with significantly higher values for maximal HR and CO. Whether these findings can be replicated in older individuals and/or those with chronic disease remains to be determined, as evoking a higher VO_{2\text{max}} in response to this newly developed protocol has great implications for the determination of VO_{2\text{max}} to quantify responses to training and establish training intensities.
Estimating Hemodynamic Responses to the Wingate Test Using Thoracic Impedance

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Abstract:
Techniques including direct Fick and Doppler echocardiography are frequently used to assess hemodynamic responses to exercise. Thoracic impedance has been shown to be a noninvasive alternative to these methods for assessing these responses during graded exercise to exhaustion, yet its feasibility during supra-maximal bouts of exercise is relatively unknown. We used thoracic impedance to estimate stroke volume (SV) and cardiac output (CO) during the Wingate test (WAnT) and compared these values to those from graded exercise testing (GXT). Active men (n = 9) and women (n = 7) (mean age = 24.8 ± 5.9 yr) completed two Wingate tests and two graded exercise tests on a cycle ergometer. During exercise, heart rate (HR), SV, and CO were continuously estimated using thoracic impedance. Repeated measures analysis of variance was used to identify potential differences in hemodynamic responses across protocols. Results: Maximal SV (138.6 ± 37.4 mL vs. 135.6 ± 26.9 mL) and CO (24.5 ± 6.1 L∙min⁻¹ vs. 23.7 ± 5.1 L∙min⁻¹) were similar (p > 0.05) between repeated Wingate tests. Mean maximal HR was higher (p < 0.01) for GXT (185 ± 7 b∙min⁻¹) versus WAnT (177 ± 11 b∙min⁻¹), and mean SV was higher in response to WAnT (177 ± 11 b∙min⁻¹), and mean SV was higher in response to WAnT (137.1 ± 32.1 mL) versus GXT (123.0 ± 32.0 mL), leading to similar maximal cardiac output between WAnT and GXT (23.9 ± 5.6 L∙min⁻¹ vs. 22.5 ± 6.0 L∙min⁻¹). Our data show no difference in hemodynamic responses in response to repeated administrations of the Wingate test. In addition, the Wingate test elicits similar cardiac output compared to progressive cycling to VO₂max.

Keywords:
• Stroke volume
• Cardiac output
• Cycle ergometer
• Maximal oxygen uptake
• Supramaximal exercise

Conclusion:
Data show no differences in repeated estimates of SV and CO obtained during the Wingate test from thoracic impedance. In addition, CO was similar although HR and SV varied between WAnT and GXT despite these bouts dramatically differing in intensity and duration, which opposes some existing data (Sagiv et al., 2000). This lack of agreement in SV and CO responses to intense exercise merits further studies investigating hemodynamic changes to acute exercise using different techniques as well as in response to chronic aerobic and interval training regimens in various populations.

Modeling the diving bradycardia: Toward an “oxygen-conserving breaking point”?

Eur J Appl Physiol
DOI 10.1007/s00421-015-3129-5

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• Frédéric Lemaître

Abstract:
Although it has been demonstrated that the exponential decay model fits the heart rate (HR) kinetics in short static breath holding (BH), this model might be inaccurate when BH is maintained for several minutes. The aim of this study was to build a new meaningful model to quantify HR kinetics during prolonged static BH. Methods Nonlinear regression analysis was used to build a model able to quantify the beat-to-beat HR reduction kinetics observed in prolonged static BH performed both in air and in immersed condition by 11 trained breath-hold divers. Dynamic changes in cardiac autonomic regulation through heart rate variability indices [root mean square of successive difference of R–R intervals (RMSSD); shortterm fractal scaling exponent: DFA α1] and peripheral oxygen saturation (SpO2) were also analyzed to strengthen the model. Results The tri-phasic model showed a sharp exponential drop in HR immediately followed by a slight linear rise up until a breaking point preceding a linear drop in HR. The breaking points had similar level of SpO2 whether in air or in immersed condition (95.1 ± 2.1 vs. 95.2 ± 3.0 %, respectively; P = 0.49), and the subsequent linear drop in HR was concomitant with a shift in cardiac autonomic regulation in air (RMSSD: +109.0 ± 47.8 %; P < 0.001; DFA α1: −18.0 ± 17.4 %; P < 0.05) and in immersion (RMSSD: +112.6 ± 55.8 %; P < 0.001; DFA α1: −26.0 ± 12 %; P < 0.001).

Conclusion:
In addition to accurately fitting the HR kinetics, the most striking finding is an “oxygen-conserving breaking point” highlighted by the model, which might be interpreted as unique adaptive feature against hypoxic damages in the human diving bradycardia.
Mixed venous oxygen saturation is impaired during maximal exercise in patients with cystic fibrosis

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Introduction:
We have recently described that patients with cystic fibrosis (CF) exhibit a reduced skeletal muscle oxidative metabolism at rest which may contribute to exercise intolerance in this population. Alterations in muscle oxidative metabolism may reduce the extraction of oxygen (O₂) by the muscle during exercise, resulting in a higher mixed venous O₂ saturation. However, whether or not this impairment is present in CF during exercise has yet to be elucidated.

Purpose:
This study sought to test the hypothesis that mixed venous O₂ saturation is higher in patients with CF compared to controls both at rest and during maximal exercise.

Methods:
Seventeen patients with CF (CF: 8 males and 9 females; 22 ± 9 years) and fifteen controls (C: 7 males and 8 females; 27 ± 8 years) volunteered for this study. An exhaustive incremental exercise test was performed on a cycle ergometer using the Godfrey protocol to determine exercise capacity (VO₂peak). Cardiac output (CO) was monitored non-invasively by Signal-Morphology Impedance Cardiology (PhysioFlow) both at rest and during maximal exercise. Mixed venous oxygen saturation (SvO₂) was determined using a derivation of the Fick equation.

Results:
VO₂ peak normalized for fat-free mass was significantly lower (p<0.001) in CF (42.2 ± 1.4 ml·kg FFM-1·min-1) compared with C (51.6 ± 1.6 ml·kg FFM-1·min-1). CO was similar at both rest (5.0 ± 0.2 vs. 5.4 ±0.2 l/min, p=0.165) and at maximal exercise (13.3 ± 0.8 vs. 15.6 ± 1.1 l/min, p=0.117) in patients with CF and C, respectively. No differences in SvO₂ were observed between groups at rest (CF: 73 ± 1 vs. C: 74 ± 2 %, p=0.651); however, SvO₂ was significantly higher (p=0.020) at maximal exercise in CF (38 ± 2%) compared with C (28 ± 4%). Additionally, a significant negative correlation was identified between SvO₂ at maximal exercise and VO₂ peak (r = -0.508, p=0.005).

Conclusion:
For the first time, we have documented a higher mixed venous O₂ saturation during maximal exercise in patients with CF that is inversely related to exercise capacity. These findings indicate that the mismatch between O₂ delivery and muscle extraction during exercise may contribute to exercise intolerance in this population. Supported in part by Vertex Pharmaceuticals IIS and NIH/NIDDK R21DK100783 (RAH).
Periodic breathing in healthy humans at exercise in hypoxia

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*Submitted 15 September 2014; accepted in final form 10 November 2014*

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**Abstract:**
Periodic breathing is frequent in heart failure or ventilatory disorders during sleep, and common during sleep at high altitude, but has been rarely studied in wakefulness and during exercise. A retrospective analysis of ventilation from hypoxia exercise tests was realized in 82 healthy subjects separated into two groups with either high or low ventilatory response to hypoxia at exercise (HVRe). A fast Fourier transform spectral analysis of the breath-by-breath ventilation ($V_E$) signal, $O_2$ saturation, and end-tidal PCO$_2$ evidenced a periodic pattern with a period of 11.1 to 12.0 s. The peak power of the $V_E$ spectrum was higher in the high HVRe group ($P<0.001$). A prospective study (25 subjects) was performed to evaluate the influence of cardiorespiratory factors on the amplitude and period of oscillations in various conditions of exercise (20 to 40% maximal aerobic power) and hypoxia (0 to 4,000 m altitude). The period of $V_E$ was shorter at exercise (vs. rest, $P<0.001$) and hypoxia (vs. normoxia, $P<0.001$), and inversely related with cardiac output and $V_E$ ($P<0.001$). $V_E$ peak power was higher at exercise ($P<0.001$) and hypoxia ($P<0.001$), and was positively related with cardiac output and $V_E$ ($P<0.001$). $V_E$ peak power in hypoxia was positively related with the ventilatory response to CO$_2$ (HCVR). This novel observation suggests that healthy subjects demonstrate a spontaneous periodic breathing, not clearly observable at rest and in normoxia, but triggered by hypoxic exercise. The periodic pattern is enhanced in subjects with high HVRe and high HCVR, suggesting that oxygen and CO$_2$ play synergistic roles in the modulation of these oscillations.

**Keywords:**
- Hypoxia
- Control of ventilation
- Periodic breathing
- Hypoxic ventilator response
- Hypercapnic ventilator response
- Exercise
### Abstract:

Periodic breathing has been found in patients with heart failure and sleep apneas, and in healthy subjects in hypoxia, during sleep and wakefulness, at rest and, recently, at exercise. To unravel the cardiorespiratory parameters liable to modulate the amplitude and period of ventilatory oscillations, 26 healthy subjects were tested under physiological (exercise) and environmental (hypoxia, hyperoxia, hyperoxic hypercapnia) stresses, and under acetazolamide (ACZ) treatment. A fast Fourier transform spectral analysis of breath-by-breath ventilation (VE) evidenced an increase in VE peak power under hypercapnia (vs. normoxia and hyperoxia, \( P < 0.001 \)) and a decrease under ACZ (vs. placebo, \( P < 0.001 \)), whereas it was not modified in hyperoxia. VE period was shortened by exercise in all conditions (vs. rest, \( P < 0.01 \)) and by hypercapnia (vs. normoxia, \( P < 0.05 \)) but remained unchanged under ACZ (vs. placebo). VE peak power was positively related to cardiac output (Qc) and VE in hyperoxia (\( P < 0.01 \)), in hypercapnia (\( P < 0.001 \)) and under ACZ (\( P < 0.001 \)). VE period was negatively related to Qc and VE in hyperoxia (\( P < 0.01 \) and \( P < 0.001 \), respectively), in hypercapnia (\( P < 0.05 \) and \( P < 0.01 \), respectively) and under ACZ (\( P < 0.05 \) and \( P < 0.01 \), respectively). Total respiratory cycle time was the main factor responsible for changes in VE period. In conclusion, exercise, hypoxia, and hypercapnia increase ventilator oscillations by increasing Qc and VE, whereas ACZ decreases ventilatory instability in part by a contrasting action on \( O_2 \) and \( CO_2 \) sensing. An intrinsic oscillator might modulate ventilation through a complex system where peripheral chemoreflex would play a key role.

### Keywords:
- Acetazolamide
- Exercise
- Hypercapnia
- Hypoxia
- Periodic breathing
- Ventilatory oscillations

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Cardiovascular Hemodynamic Response to the Normal and Pathologic Human Diving Reflex

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Purpose:  
This study followed our award winning clinical abstract from ACSM 2015. Human diving reflex is well known reaction of the cold water immersion. However only limited data are available for those cases, when clinically significant case appears. The aim of the study was to monitor hemodynamic response for two groups of individuals - one with physiologically appropriate reaction, and second with pathological reaction manifested by clinically relevant symptoms.

Methods:  
Two groups of individuals were monitored during cold water face immersion. Each individual placed the face into the cold water (7oC) immersion until exhaustion. The test has been repeated three times for each individual. The cardiovascular hemodynamic parameters were monitored via 12 lead ECG and noninvasive bio-impedance system PhysioFlow. The following parameters were recorded: heart rate (HR), stroke volume (SV), cardiac output (CO), and systemic vascular resistance (SVR).

Results:  
2 individuals with symptomatic pathology (presyncope, dizziness or dyscoordination during swimming) and 5 normal individuals were included. All together 21 measurements were recorded. The detailed information are included in the following table:

<table>
<thead>
<tr>
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<th>HR (BPM)</th>
<th>SV (ml)</th>
<th>CO (L/min)</th>
<th>SVR (dyn.s/cm²)</th>
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<td>Pathologic</td>
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<tr>
<td>response</td>
<td>Mean</td>
<td>88</td>
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Conclusion:  
Our study demonstrated for the first time, that pathological (overshoot) response to the face water immersion is not only manifested by severe bradycardia. This is rather a whole body circulatory collapse with clinically relevant drop in heart rate and stroke volume resulting in insufficient cardiac output, compensated by global systemic vasoconstriction. Results might help us to understand better possible causes of the sudden death of swimmers and triathlon racers.
3. Research

3.1 Physiology

Histamine H₂ receptor blockade augments blood pressure responses to acute submaximal exercise in males

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• Jong-Kyung Kim

Abstract:
Histamine is a potent vasodilator that has been found to increase during exercise. We tested the hypothesis that histamine would attenuate blood pressure (BP), cardiac output (CO), and vascular resistance responses to short-term, submaximal dynamic exercise during H₂ receptor blockade. Fourteen healthy men (20–29 years of age) were studied. Systolic (SBP), diastolic (DBP), and mean arterial (MAP) BP and heart rate (HR) were assessed at rest and during the last minute of 10 min of submaximal cycling exercise (60% of peak oxygen consumption) in the absence and presence of histamine H₂ receptor blockade (ranitidine, 300 mg). Stroke volume (SV) (impedance cardiography) and plasma norepinephrine (NE) were measured, and CO, rate × pressure product (RPP), and total peripheral resistance (TPR) were calculated. Plasma levels of histamine were also measured. H₂ blockade had no effects on any variables at rest. During exercise, SBP (184±3mmHg vs. 166±2mmHg), MAP (121 ± 2mmHg vs. 112±5mmHg), and RPP (25.9 ± 0.8 × 10³mmHg·beats/min vs. 23.5 ± 0.8 × 10³mmHg·beats·min) were greater during blocked conditions (P < 0.05), and an interaction was observed for TPR. SV, DBP, HR, and NE levels were unaffected by blockade. Plasma histamine increased from 1.83 ± 0.14 ng/mL at rest to 2.33 ± 0.23 ng/mL during exercise (P < 0.05) and was not affected by H₂ blockade (1.56 ± 0.23 ng/mL vs. 1.70 ± 0.24 ng/mL). These findings suggest that, during submaximal exercise, histamine attenuates BP, vascular resistance, and the work of the heart via activation of H₂ receptors and that these effects occurred primarily in the vasculature and not in the myocardium.

Conclusion:
The results of this study demonstrate that histamine can act on H₂ receptors to attenuate BP, TPR, and RPP in male subjects during short-term submaximal exercise that is capable of causing increases in plasma histamine. Because these effects occur in the absence of changes in HR, SV, and CO, it appears that there is also a redistribution of CO whereby increases in blood flow in some regional circulations are offset by decreases in others. Consequently, we suggest that, during short-term submaximal exercise, histamine mediates peripheral vasodilation, which limits increases in BP and afterload and lowers cardiac workload, effects that lessen stress on the heart.
Effects of chronic dietary nitrate supplementation on the hemodynamic response to dynamic exercise


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Abstract:
Effects of chronic dietary nitrate supplementation on the hemodynamic response to dynamic exercise. Am J Physiol Regul Integr Comp Physiol 309: R459–R466, 2015. First published June 17, 2015; doi:10.1152/ajpregu.00099.2015.—While acute treatment with beetroot juice (BRJ) containing nitrate (NO3) can lower systolic blood pressure (SBP), afterload, and myocardial O2 demand during submaximal exercise, effects of chronic supplementation with BRJ (containing a relatively low dose of NO3, 400 mg) on cardiac output (CO), SBP, total peripheral resistance (TPR), and the work of the heart in response to dynamic exercise are not known. Thus, in 14 healthy males (22 ± 1 yr), we compared effects of 15 days of both BRJ and nitrate-depleted beetroot juice (NDBRJ) supplementation on plasma concentrations of NOx (NO3/NO2), SBP, diastolic blood pressure (DBP), mean arterial pressure (MAP), CO, TPR, and rate pressure product (RPP) at rest and during progressive cycling exercise. Endothelial function was also assessed via flow-mediated dilation (FMD). BRJ supplementation increased plasma NOx from 83.8 ± 13.8 to 167.6 ± 13.2 µM. Compared with NDBRJ, BRJ reduced SBP, DBP, MAP, and TPR at rest and during exercise (P < 0.05). In addition, RPP was decreased during exercise, while CO was increased, but only at rest and the 30% workload (P < 0.05). BRJ enhanced FMD induced increases in brachial artery diameter (pre: 12.3 ± 1.6%; post: 17.8 ± 1.9%). We conclude that 1) chronic supplementation with BRJ lowers blood pressure and vascular resistance at rest and during exercise and attenuates RPP during exercise and 2) these effects may be due, in part, to enhanced endothelium-induced vasodilation in contracting skeletal muscle. Findings suggest that BRJ can act as a dietary nutraceutical capable of enhancing O2 delivery and reducing work of the heart, such that exercise can be performed at a given workload for a longer period of time before the onset of fatigue.

Results:
Physical characteristics of the subjects are shown in Table 1. Table 2 presents effects of BRJ supplementation on plasma NOx and brachial artery FMD. BRJ supplementation caused significant increases in resting plasma NOx concentrations and in FMD. NDBRJ supplementation had no effect on NOx concentrations or FMD. FMD was positively correlated to NOx concentrations (r = 0.4; P < 0.05). Absolute values of all hemodynamic variables at rest and during the 30%, 60%, and 80% of VO2peak workloads were not altered by NDBRJ supplementation. Compared with pretreatment conditions, BRJ supplementation reduced SAP, DBP, MAP, and TPR at rest and during all workloads, while RPP was attenuated at every workload (P < 0.05) (Figs. 1 and 2). No effects of BRJ on HR were seen (Fig. 1). SV was higher at rest and at the 30% and 60% of VO2peak workloads after BRJ supplementation, while CO was elevated at rest and during exercise at the 30% of VO2peak workload (P < 0.05) (Fig. 2). Absolute values of all hemodynamic variables at rest and during all workloads were similar when compared between pre-NDBRJ and pre-BRJ supplementation conditions. When compared with NDBRJ supplementation, BRJ attenuated SBP, DBP, MAP, and RPP responses at rest and during exercise (P < 0.05) (Figs. 3 and 4). In addition, BRJ augmented SV and attenuated TPR at rest and during the 30% and 60% VO2peak Workloads and augmented CO at the workloads of 30% and 60% of VO2peak (P < 0.05) (Fig. 4). No differences in HR were found between the two conditions at rest or across any workload (Fig. 3).
Single session of sprint interval training elicits similar cardiac output but lower oxygen uptake versus ramp exercise to exhaustion in men and women

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Abstract:
Sprint interval training (SIT) elicits comparable long-term adaptations versus continuous exercise training (CEX) including increased maximal oxygen uptake (VO$_{2}$max) and fat utilization. However, there is limited research examining acute hemodynamic responses to SIT. The aim of this study was to examine hemodynamic responses to low-volume SIT. Active men (n=6, VO$_{2}$max = 39.8 ± 1.7 mL/kg/min) and women (n=7, VO$_{2}$max = 37.3 ± 5.7 mL/kg/min) performed a ramp-based VO2max test (RAMP) to determine workload for the SIT session. Subjects returned within 1 wk and completed a session of SIT consisting of six 30-s bouts of “all-out” cycling at 130% maximal workload (Wmax) interspersed with 120 s of active recovery. Continuously during RAMP and exercise and recovery in SIT, VO$_{2}$ was obtained and thoracic impedance was used to estimate heart rate (HR), stroke volume (SV), and cardiac output (CO). Results revealed no significant differences in COmax (p = 0.12, 19.7 ± 2.4 L/min vs. 20.3 ± 1.8 L/min) but lower SVmax (p = 0.004, 110.4 ± 15.7 mL vs. 119.4 ± 15.5 mL) in RAMP versus SIT. HRmax from SIT (179.0 ± 11.8 b/min) was lower (p = 0.008) versus RAMP (184.4 ± 7.9 b/min). Peak VO2 (L/min) was lower (p < 0.001) in response to SIT (2.43 ± 0.82 L/min) compared to RAMP (2.84 ± 0.82 L/min). Hemodynamic variables increased linearly across SIT bouts and remained significantly elevated in recovery. Sprint interval training consisting of 3 min of supramaximal exercise elicits similar CO yet lower VO$_{2}$ compared to RAMP.
High-Intensity Interval Training Increases Cardiac Output and VO2max

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Purpose:
This study examined changes in VO2max and cardiac output (CO) in response to periodized HIIT.

Methods:
Thirty-nine active men and women (mean age and VO2max = 22.9 ± 5.4 yr and 39.6 ± 5.6 mL kg⁻¹min⁻¹) performed HIIT and 32 men and women (age and VO2max = 25.7 ± 4.5 yr and 40.7 ± 5.2 mL kg⁻¹min⁻¹) were nonexercising controls (CON). The first 10 sessions of HIIT required eight to ten 60 s bouts of cycling at 90%–110% percent peak power output interspersed with 75 s recovery, followed by randomization to one of three regimes (sprint interval training (SIT), high-volume interval training (HIITHI), or periodized interval training (PER) for the subsequent 10 sessions. Before, midway, and at the end of training, progressive cycling to exhaustion was completed during which VO2max and maximal CO were estimated.

Results:
Compared with CON, significant (P<0.001) increases in VO2max in HIIT + SIT (39.8 ± 7.3 mL kg⁻¹min⁻¹ to 43.6 ± 6.1 mL kg⁻¹min⁻¹), HIIT + HIITHI (41.1 ± 4.9 mL kg⁻¹min⁻¹ to 44.6 ± 7.0 mL kg⁻¹min⁻¹), and HIIT + PER (39.5 ± 5.6 mL kg⁻¹min⁻¹ to 44.1 ± 5.4 mL kg⁻¹min⁻¹) occurred which were mediated by significant increases in maximal CO (20.0 ± 3.1 L min⁻¹ to 21.7 ± 3.2 L min⁻¹, P = 0.04). Maximal stroke volume was increased with HIIT (P = 0.04), although there was no change in maximal HR (P = 0.88) or arteriovenous O2 difference (P = 0.36).

Conclusion:
Increases in VO2max exhibited in response to different HIIT regimes are due to improvements in oxygen delivery.
Influence of Active Recovery on Cardiovascular Function During Ice Hockey

DOI 10.1186/s40798-015-0026-8

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Abstract:

Background: Ice hockey is a popular sport comprised of high-intensity repeated bouts of activity. Light activity, as opposed to passive rest, has been shown to improve power output in repeated sprinting and could potentially help to offset venous pooling, poor perfusion, and the risk of an ischemic event. The objective of our study was, thus, to examine the efficacy of low-intensity lower body activity following a simulated hockey shift for altering hemodynamic function.

Methods: In a cross-over design, 15 healthy hockey players (23 ± 1 years, 54 ± 3 mL/kg/min) performed two simulated hockey shifts. In both conditions, players skated up to 85 % of age-predicted heart rate maximum, followed by either passive recovery or active recovery while hemodynamic measures were tracked for up to 180 s of rest.

Results: Light active recovery within the confines of an ice hockey bench, while wearing skates and protective gear, was effective for augmenting cardiac output (an average of 2.5 ± 0.2 L/min, p = 0.03) at 45, 50, and 120 s. These alterations were driven by a sustained elevation in heart rate (12 bpm, p = 0.05) combined with a physiological relevant but non-significant (11.6 mL, p = 0.06) increase in stroke volume.

Conclusion:
Standing and pacing between shifts offers a realistic in-game solution to help slow the precipitous drop in cardiac output (heart rate and stroke volume) that typically occurs with passive rest. Prolonging the duration of an elevated cardiac output further into recovery may be beneficial for promoting recovery of the working skeletal muscles and also avoiding venous pooling and reduced myocardial perfusion.
Physiological Comparison of Concentric and Eccentric Arm Cycling In Males and Females

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Abstract:
Lower body eccentric exercise is well known to elicit high levels of muscular force with relatively low cardiovascular and metabolic strain. As a result, eccentric exercise has been successfully utilised as an adaptive stressor to improve lower body muscle function in populations ranging from the frail and debilitated, to highly-trained individuals. Here we investigate the metabolic, cardiorespiratory, and energy costs of upper body eccentric exercise in a healthy population. Seven men and seven women performed 4-min efforts of eccentric (ECC) or concentric (CON) arm cycling on a novel arm ergometer at workloads corresponding to 40, 60, and 80% of their peak workload as assessed in an incremental concentric trial. The heart rate, ventilation, cardiac output, respiratory exchange ratio, and blood lactate concentrations were all clearly greater in CON condition at all of the relative workloads (all p<0.003). Effect size calculations demonstrated that the magnitude of the differences in VO2 and work economy between the ECC and CON exercise ranged from very large to extremely large; however, in no case did mechanical efficiency (ηMECH) differ between the conditions (all p>0.05). In contrast, delta efficiency (ηΔ), as previously defined by Coyle and colleagues in 1992, demonstrated a sex difference (men>women; p<0.05). Sex differences were also apparent in arteriovenous oxygen difference and heart rate during CON. Here, we reinforce the high-force, low cost attributes of eccentric exercise which can be generalised to the muscles of the upper body. Upper body eccentric exercise is likely to form a useful adjunct in debilitative, rehabilitative, and adaptive clinical exercise programs; however, reports of a shift towards an oxidative phenotype should be taken into consideration by power athletes. We suggest delta efficiency as a sensitive measure of efficiency that allowed the identification of sex differences.
Central and peripheral adjustments during high-intensity exercise following cold water immersion


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_ Springer-Verlag Berlin Heidelberg 2013

**Authors:**
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• Jeff S. Coombes,
• Martin Buchheit

**Abstract:**
Purpose We investigated the acute effects of cold water immersion (CWI) or passive recovery (PAS) on physiological responses during high-intensity interval training (HIIT).

Methods In a crossover design, 14 cyclists completed 2 HIIT sessions (HIIT1 and HIIT2) separated by 30 min. Between HIIT sessions, they stood in cold water (10 _C) up to their umbilicus, or at room temperature (27 _C) for 5 min. The natural logarithm of square-root of mean squared differences of successive R–R intervals (ln rMSSD) was assessed pre- and post-HIIT1 and HIIT2. Stroke volume (SV), cardiac output ( _Q), O2 uptake ( _VO2), total muscle hemoglobin (tHb) and oxygenation of the vastus lateralis were recorded (using near infrared spectroscopy); heart rate, _Q, and _V O2 on-kinetics (i.e., mean response time, MRT), muscle de-oxygenation rate, and anaerobic contribution to exercise were calculated for HIIT1 and HIIT2.

Results ln rMSSD was likely higher [between-trial difference (90 % confidence interval) [?13.2 % (3.3; 24.0)] after CWI compared with PAS. CWI also likely increased SV [?5.9 % (-0.1; 12.1)], possibly increased _Q [?4.4 % (-1.0; 10.3)], possibly slowed _Q MRT [?18.3 % (-4.1; 46.0)], very likely slowed _V O2 MRT [?16.5 % (5.8; 28.4)], and likely increased the anaerobic contribution to exercise [?9.7 % (-1.7; 22.5)].

**Conclusion:**
CWI between HIIT slowed _V O2 on-kinetics, leading to increased anaerobic contribution during HIIT2. This detrimental effect of CWI was likely related to peripheral adjustments, because the slowing of _VO2 on-kinetics was twofold greater than that of central delivery of O2 (i.e., _Q). CWI has detrimental effects on high-intensity aerobic exercise performance that persist for C45 min.
Effects of cold water immersion and active recovery on hemodynamics and recovery of muscle strength following resistance exercise

Submitted 14 April 2015; accepted in final form 8 June 2015

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Abstract:

Effects of cold water immersion and active recovery on hemodynamics and recovery of muscle strength following resistance exercise. Am J Physiol Regul Integr Comp Physiol 309: R389–R398, 2015. First published June 15, 2015; doi:10.1152/ajpregu.00151.2015.—Cold water immersion (CWI) and active recovery (ACT) are frequently used as postexercise recovery strategies. However, the physiological effects of CWI and ACT after resistance exercise are not well characterized. We examined the effects of CWI and ACT on cardiac output (Q˙), muscle oxygenation (SmO2), blood volume (tHb), muscle temperature (Tmuscle), and isometric strength after resistance exercise. On separate days, 10 men performed resistance exercise, followed by 10 min CWI at 10°C or 10 min ACT (low-intensity cycling). Q˙ (7.9 ± 2.7 l) and Tmuscle (2.2 ± 0.8°C) increased, whereas SmO2 (-21.5 ± 8.8%) and tHb (-10.1 ± 7.7 µM) decreased after exercise (P < 0.05). During CWI, Q˙ (-1.1 ± 0.7l) and Tmuscle (-6.6 ± 5.3°C) decreased, while tHb (121 ± 77µM) increased (P < 0.05). In the hour after CWI, Q˙ and Tmuscle remained low, while tHb also decreased (P < 0.05). By contrast, during ACT, Q˙ (3.9 ± 2.3 l), Tmuscle (2.2 ± 0.5°C), SmO2 (17.1 ± 5.7%), and tHb (91 ± 66 µM) all increased (P < 0.05). In the hour after ACT, Tmuscle, and tHb remained high (P < 0.05). Peak isometric strength during 10-s maximum voluntary contractions (MVCs) did not change significantly after CWI, whereas it decreased after ACT (~30 to -45 Nm; P < 0.05). Muscle deoxygenation time during MVCs increased after ACT (P < 0.05), but not after CWI. Muscle reoxygenation time after MVCs tended to increase after CWI (P < 0.052). These findings suggest first that hemodynamics and muscle temperature after resistance exercise are dependent on ambient temperature and metabolic demands with skeletal muscle, and second, that recovery of strength after resistance exercise is independent of changes in hemodynamics and muscle temperature.

Keywords:

• cryotherapy;
• muscle oxygenation;
• blood flow;
• recovery
Associations between G tolerance and changes of stroke volume, heart rate, and cardiac output in operation anti-G straining maneuver

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Introduction:
The purpose of performing anti-G straining maneuver (AGSM) is to increase cardiac output (CO) and ultimately, blood supply to the brain, to avoid black out and G-induced loss of consciousness (G-LOC) during high G air combat maneuvers. Until now, the effectiveness of AGSM performed by trainees in Taiwan is evaluated subjectively.

Aims:
To investigate the association between G tolerance and cardiac performance parameters while performing AGSM on the ground and during high G endurance training.

Methods:
This is a longitudinal study design. Young male volunteers were randomly recruited from 2015 flights surgeons/aviation physiologist training program. Cardiac performance parameters (cardiac output, CO; stroke volume, SV and heart rate, HR) were evaluated using non-invasive instrumentation (PhysioFlow® Enduro™ Manatec Biomedical, Paris, France) on the ground at 1G and during high G endurance training in a human centrifuge (Latécoère, France).

Results and Conclusion:
Five young male (age, 27.8 ± 2.8 years; body mass index, 23.8 ± 3.3) participated in the study. Their mean relaxed and straining G tolerance were 4.7 and 8.6 G, respectively. The effectiveness of AGSM (G increment or gain) was 3.9 G. Ratios of SV, HR, CO between high G training and ground training while performing AGSM were 1.09, 0.94 and 0.95, respectively. During training, three subjects non-G-LOC group (n=3) were 1.2, 0.92 and 0.98, respectively while those in the G-LOC group (n=2) were 0.93, 0.97 and 0.89, respectively. When comparing AGSM effectiveness, ratios of SV, HR, CO in G increment ≥ 4G group (n=3) were 1.19, 0.98 and 1.08, respectively while those in G increment < 4G group (n=2) were 0.94, 0.88 and 0.75, respectively. We were able to measure cardiac performance during centrifuge training with non-invasive methodology. In the future, we will recruit air force cadets into our study to pursue our final aim.

Aerospace medicine and human performance, vol.87, N°1 March 2016, P.315
Low haemoglobin concentration in Tibetan males is associated with greater high-altitude exercise capacity

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Abstract:
Tibetans living at high altitude have adapted genetically such that many display a low erythropoietic response, resulting in near sea-level haemoglobin (Hb) concentration. We hypothesized that absence of the erythropoietic response would be associated with greater exercise capacity compared to those with high [Hb] as a result of beneficial changes in oxygen transport. We measured, in 21 Tibetan males with [Hb] ranging from 15.2 g dl$^{-1}$ to 22.9 g dl$^{-1}$ (9.4 mmol l$^{-1}$ to 14.2 mmol l$^{-1}$), [Hb], ventilation, volumes of O$_2$ and CO$_2$ utilized at peak exercise ($V_O_2$ and $V_CO_2$), heart rate, cardiac output and arterial blood gas variables at peak exercise on a cycle ergometer at $\sim$4200 m. Lung and muscle O$_2$ diffusional conductances were computed from these measurements. [Hb] was related (negatively) to $V_O_2$ kg$^{-1}$ ($r = -0.45$, $P<0.05$), cardiac output kg$^{-1}$ (QT kg$^{-1}$, $r = -0.54$, $P < 0.02$), and O$_2$ diffusion capacity in muscle (DM kg$^{-1}$, $r = -0.44$, $P<0.05$), but was unrelated to ventilation, arterial partial pressure of O$_2$ ($P_{SO_2}$) or pulmonary diffusing capacity. Using multiple linear regression, variance in peak $V_O_2$.kg$^{-1}$ was primarily attributed to QT, DM, and $P_{CO_2}$.($R^2 = 0.88$). However, variance in pulmonary gas exchange played essentially no role in determining peak $V_O_2$. These results (1) show higher exercise capacity in Tibetans without the erythropoietic response, supported mostly by cardiac and muscle O$_2$ transport capacity and ventilation rather than pulmonary adaptations, and (2) support the emerging hypothesis that the polycythaemia of altitude, normally a beneficial response to low cellular $P_O_2$, may become maladaptive if excessively elevated under chronic hypoxia. The cause and effect relationships among [Hb], QT, DM, and $P_{CO_2}$ remain to be elucidated.

Conclusion:
At altitude >4000 m, Tibetan males with sea-level [Hb], compared to those with elevated [Hb], exhibit greater exercise capacity, higher cardiac output, and greater O2 diffusional conductance in muscle but not lung. These components as well as PaCO2 are further associated with exercise capacity. The physiological and genetic relationships among [Hb], cardiac function and muscle O2 diffusional conductance remain to be elucidated. Supplemental (100%) O2 given during exercise increases peak work rate in Tibetans by only a third of that reported in Caucasian lowlanders acclimatized to altitude (with no difference between high and low [Hb] groups). Acclimatized Han Chinese males performed similarly in terms of exercise capacity and components of O2 transport to the high [Hb] Tibetan group, suggesting a lack of adaptive changes in these groups. As indicated in many reports, the fact that healthy Andeans are polycythaemic at altitude, while many Amhara Ethiopians and Tibetans are not, suggests distinct evolutionary paths between these native highland groups.
Impact of Polyphenol Antioxidants on Cycling Performance and Cardiovascular Function


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- Edward F. Coyle

**Abstract:**
This investigation sought to determine if supplementation with polyphenol antioxidant (PA) improves exercise performance in the heat (31.5 °C, 55% RH) by altering the cardiovascular and thermoregulatory responses to exercise. Twelve endurance trained athletes ingested PA or placebo (PLAC) for 7 days. Consecutive days of exercise testing were performed at the end of the supplementation periods. Cardiovascular and thermoregulatory measures were made during exercise. Performance, as measured by a 10 min time trial (TT) following 50 min of moderate intensity cycling, was not different between treatments (PLAC: 292 ± 33 W and PA: 279 ± 38 W, $p = 0.12$). Gross efficiency, blood lactate, maximal neuromuscular power, and ratings of perceived exertion were also not different between treatments. Similarly, performance on the second day of testing, as assessed by time to fatigue at maximal oxygen consumption, was not different between treatments (PLAC; 377 ± 117 s vs. PA; 364 ± 128 s, $p = 0.61$). Cardiovascular and thermoregulatory responses to exercise were not different between treatments on either day of exercise testing. Polyphenol antioxidant supplementation had no impact on exercise performance and did not alter the cardiovascular or thermoregulatory responses to exercise in the heat.

**Keywords:**
- thermoregulation
- exercise
- antioxidant

**Conclusion:**
Based on the findings of this study, polyphenol antioxidant supplementation had no beneficial effect on performance during both prolonged and short duration exhaustive exercise in the heat in endurance-trained cyclists. Accordingly, polyphenol antioxidant supplementation had no effect on gross cycling efficiency, rating of perceived exertion, or the cardiovascular and thermoregulatory responses to exercise. Overall, these findings question the use of polyphenol antioxidant supplementation as an ergogenic aid aimed at improving endurance exercise performance.
## 3.2 PHARMACOLOGY

**Pharmacology**

Ephedrine Fails to Accelerate the Onset of Neuromuscular Block by Vecuronium

*Anesth Analg 2003; 97:480-483*

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<tr>
<td>Ryu Komatsu, MD¹, Osamu Nagata, MD¹, Makoto Ozaki, MD¹, Daniel I. Sessler, MD²</td>
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**Abstract:**

The onset time of neuromuscular blocking drugs is partially determined by circulatory factors, including muscle blood flow and cardiac output. We thus tested the hypothesis that a bolus of ephedrine accelerates the onset of vecuronium neuromuscular block by increasing cardiac output. A prospective, randomized study was conducted in 53 patients scheduled for elective surgery. After the induction of anesthesia, the ulnar nerve was stimulated supramaximally every 10 s, and the evoked twitch response of the adductor pollicis was recorded with accelerometry. Patients were maintained under anesthesia with continuous infusion of propofol for 10 min and then randomly assigned to ephedrine 210 µg/kg (n = 27) or an equivalent volume of saline (n = 26). The test solution was given 1 min before the administration of 0.1 mg/kg of vecuronium. Cardiac output was monitored with impedance cardiography. Ephedrine, but not saline, increased cardiac index (17%; P = 0.003). Nonetheless, the onset of 90% neuromuscular block was virtually identical in the patients given ephedrine (183 ± 41 s) and saline (181 ± 47 s). There was no correlation between cardiac index and onset of the blockade. We conclude that the onset of the vecuronium-induced neuromuscular block is primarily determined by factors other than cardiac output. The combination of ephedrine and vecuronium thus cannot be substituted for rapid-acting nondepolarizing muscle relaxants.

**Implication:**

Ephedrine increased cardiac index but failed to speed onset of neuromuscular block with vecuronium. We conclude that ephedrine administration does not shorten the onset time of vecuronium.
Short-term Vasomotor Adjustments to Post Immersion Dehydration are Hindered by Natriuretic Peptides

Abstract:
Short-term vasomotor adjustments to post immersion dehydration are hindered by natriuretic peptides. Undersea Hyperb Med 2004, 31(2):000-000. Many studies have described the physiology of water immersion (WI), whereas few have focused on post WI physiology, which faces the global water loss of the large WI diuresis. Therefore, we compared hemodynamics and vasomotor tone in 10 trained supine divers before and after two 6h sessions in dry (DY) and head out WI environments. During each exposure (DY and WI) two exercise periods (each one hour 75W ergometer cycling) started after the 3rd and 5th hours. Weight losses were significant (-2.24 ± 0.13 kg and -2.38 ± 0.19 kg, after DY and WI, respectively), but not different between the two conditions. Plasma volume was reduced at the end of the two conditions (-9.7 ± 1.6 % and -14.7 ± 1.6 %, respectively; p<0.05). This post-WI decrease was deeper than post DY (p<0.05). Cardiac output (CO) and mean arterial blood pressure were maintained after the two exposures. Plasma levels of noradrenaline, antidiuretic hormone and ANP were twofold higher after WI than after DY (p<0.05). After DY total peripheral resistances (TPR) were increased (p<0.05) and heart rate (HR) was reduced (p<0.05). After WI there was a trend for a decrease in stroke volume (p=0.07) with unchanged TPR and HR, despite more sizeable increases in plasma noradrenaline and vasopressin than after DY. We hypothesized that the higher levels of plasma natriuretic peptides after WI were likely counteracting the dehydration-required vasomotor adjustments.
Sildenafil Inhibits Altitude-induced Hypoxemia and Pulmonary Hypertension

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Abstract:
Exposure to high altitude induces pulmonary hypertension that may lead to life-threatening conditions. In a randomized, double-blind, placebo-controlled study, the effects of oral sildenafil on altitude-induced pulmonary hypertension and gas exchange in normal subjects were examined. Twelve subjects (sildenafil [SIL] n = 6; placebo [PLA] n = 6) were exposed for 6 days at 4,350 m. Treatment (3 x 40 mg/day) was started 6 to 8 hours after arrival from sea level to high altitude and maintained for 6 days. Systolic pulmonary artery pressure (echocardiography) increased at high altitude before treatment (+29% versus sea level, p < 0.01), then normalized in SIL (-6% versus sea level, NS) and remained elevated in PLA (+21% versus sea level, p < 0.05). Pulmonary acceleration time decreased by 27% in PLA versus 6% in SIL (p < 0.01). Cardiac output and systemic blood pressures increased at high altitude then decreased similarly in both groups. PaO₂ was higher and alveolar-arterial difference in O₂ lower in SIL than in PLA at rest and exercise (p < 0.05). The altitude-induced decrease in maximal O₂ consumption was smaller in SIL than in PLA (p < 0.05). Sildenafil protects against the development of altitude-induced pulmonary hypertension and improves gas exchange, limiting the altitude-induced hypoxemia and decrease in exercise performance.

Keywords:
• Cardiac output,
• Exercise,
• Gas exchange,
• Hypoxia

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### Abstract:
Sildenafil causes pulmonary vasodilation, thus potentially reducing impairments of hypoxia-induced pulmonary hypertension on exercise performance at altitude. The purpose of this study was to determine the effects of Sildenafil during normoxic and hypoxic exercise. We hypothesized that 1) sildenafil would have no significant effects on normoxic exercise, and 2) Sildenafil would improve cardiac output, arterial oxygen saturation, and performance during hypoxic exercise.

Ten trained males performed 1 practice and 3 experimental trials at sea level (SL) and simulated high altitude (HA) of 3,874 m. Each cycling test consisted of a set work rate portion (55% Watts_{peak}: 1 h SL, 30 min HA) followed immediately by a time-trial (10 km SL, 6 km HA). Double-blinded capsules (placebo, 50, or 100 mg) were taken 1 h prior to exercise in a randomly, counterbalanced order. For HA testing, subjects also began breathing hypoxic gas (12.8% O_{2}) 1 h prior to exercise. At SL, Sildenafil had no effects on any cardiovascular or performance measures. At HA, Sildenafil increased stroke volume (measured by electrical impedance cardiography), cardiac output (Q), and arterial oxygen saturation (Sao_{2}) during set work rate exercise. Sildenafil lowered 6 km time-trial time by 15% (P < 0.05). Sao_{2} was also higher during the time trial (P < 0.05) in response to Sildenafil, despite higher work rates. Post-hoc analyses revealed two subject groups, Sildenafil responders and non-responders, who improved time-trial performance by 39% (P < 0.05) and 1.0%, respectively. No dose-response effects were observed. During cycling exercise in acute hypoxia, Sildenafil can greatly improve cardiovascular function, arterial oxygen saturation, and performance for certain individuals.

### Keywords:
- Phosphodiesterase-5 inhibitor
- Simulated altitude
- Viagra
- Physioflow
- Pulmonary hypertension
Side-effects of L-dopa on Venous Tone in Parkinson's Disease: a Leg-weighing Assessment

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Abstract:
In the present study, the effects of L-dopa treatment on cardiovascular variables and peripheral venous tone were assessed in 13 patients with Parkinson's disease (PD) with Hoehn and Yahr stages 1–4. Patients were investigated once with their regular treatment and once after 12 h of interruption of L-dopa treatment. L-Dopa intake significantly reduced systolic and diastolic blood pressure, heart rate and plasma noradrenaline and adrenaline in both the supine and upright (60°) positions. A significant reduction in stroke volume and cardiac output was also seen with L-dopa. The vascular status of the legs was assessed through thigh compression during leg weighing, a new technique developed in our laboratory. Healthy subjects were used to demonstrate that this technique provided reproducible results, consistent with those provided by strain gauge plethysmography of the calf. When using this technique in patients with PD, L-dopa caused a significant lowering of vascular tone in the lower limbs as shown, in particular, by an increase in venous distensibility. Combined with the results of the orthostatic tilting, these findings support that the treatment-linked lowering of plasma noradrenaline in patients with PD was concomitant with a significant reduction in blood pressure, heart rate and vascular tone in the lower limbs. These pharmacological side-effects contributed to reduce venous return and arterial blood pressure which, together with a lowered heart rate, worsened the haemodynamic status.

Keywords:
• Nitroglycerine,
• Noradrenaline,
• Orthosympathetic control,
• Parkinson's disease,
• Vascular tone,
• Vascular plethysmography

Abbreviations:
AFI: arterial flow index;
BP: blood pressure;
CO: cardiac output;
C_slope: slope of compliance;
CV: coefficient of variation;
DBP: diastolic BP;
HR: heart rate;
NG: nitroglycerine;
PD: Parkinson's disease;
SBP: systolic BP;
SGP: strain gauge plethysmography;
SV: stroke volume;
TC: thigh compression;
VDI: venous distensibility index
Influence of beta-blocker on cardiac output in a maximum exercise bicycle ramp test.

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Abstract:


Keywords:

- Arterial hypertension
- Students, exercise test
- Cardiac output
- Bisoprolol
- Beta blocker

Objective:

One of the most important risk factors for illness of the heart-circulation-system is arterial hypertension (8). In this study, the influence of Beta-Blocker on exercise and cardiac output (CO) in the special collective of the students was investigated.

Material & Methods:

5 students (age mean=25,4 yrs, BMI mean=23.98 kg/m2, RRrest mean=141,2/80,8 mmHg) with hypertension and pre-hypertension and no history of respiratory disease of the University of Leipzig participated in the study. The participants performed 2 maximum exercise tests. The first test was without medical intervention the second test was performed after 3 days of received 5mg/d bisoprolol. For analyzing the CO we used the system ”PhysioFlow” which is based on an impedance technology.

The results were analyzed from 0% to 100% of maximum work load using 10% intervals and during recovery after the 1\textsuperscript{st}, 3\textsuperscript{rd} and 5\textsuperscript{th} minute.

Results:

- beta blocker does not influence cardiac output
- beta blocker does not influence maximum workload
- beta blocker does not influence maximum oxygen uptake
Evaluation of a method utilizing PhysioFlow®, a novel signal morphology-based form of impedance cardiography, to measure cardiac output in the conscious beagle

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Abstract:
Currently, standard methods for measuring cardiac output are either invasive (i.e. flowprobe) or are limited in terms of short measurement intervals and measurement variability (i.e. echocardiography). The ability to reliably measure cardiac output in a non-invasive manner in large animals would provide a valuable tool to expand functional cardiovascular endpoints in preclinical safety studies. PhysioFlow® is a novel method that uses waveform analysis of an impedance signal to measure cardiac output non-invasively. Unlike cardiac impedance techniques in the past, PhysioFlow® is not dependent on thoracic structure or basal thoracic impedance (Z₀) and therefore this methodology is transferrable from human to animal models.

Keywords:
• Acepromazine
• Beagle
• Cardiac output
• Dobutamine
• Dog
• Methods
• Minoxidil
• PhysioFlow®

Methods:
Three tool compounds with known effects on cardiac output were administered to conscious beagle dogs to determine if the non-invasive PhysioFlow® system could detect the expected changes in stroke volume and cardiac output as determined by literature references using the current standard methodologies (e.g. aortic blood flow and thermodilution).

Conclusion:
The PhysioFlow® system was able to detect increases in cardiac output when dosed with 20 μg/kg of Dobutamine, a decrease in cardiac output when dosed with 0.1 mg/kg of Acepromazine, and no significant change in cardiac output when dosed with 2 mg/kg of Minoxidil. These results are within expected ranges based on published literature (Stepien et al., 1995; Taylor et al., 2007).

Discussion:
PhysioFlow®, a signal morphology-based impedance cardiography, can be utilized to reliably and non-invasively measure cardiac output in beagle dogs.

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4. Eorta/Vascular stiffness

4

EORTA/VASCULAR STIFNESS
4.1 EORTA/VASCULAR STIFFNESS

Assessment of aortic stiffness by local and regional methods

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Abstract:
The stiffness of large arteries has an important role in cardiovascular hemodynamics. Aortic stiffness (AoStiff) can be assessed non-invasively with regional and local methods. In this paper, we compared these two techniques for evaluating AoStiff. Our subjects comprised of 118 consecutive patients (85 men, mean age: 49±14 years). We evaluated regional AoStiff with carotid-femoral pulse wave velocity (PWV) measured with a tonometric technique and by bioelectrical impedance (BI) wave velocity (IWV). The local AoStiff was calculated from BI signals recorded at the chest. We used glyceryl trinitrate (GTN) to test the effect of peripheral vasodilatation on both methods in a subgroup of 52 patients (37 men, mean age: 52±11 years).
We found a significant correlation between IWV and PWV measurements ($r=0.88$, $P<0.0001$) as well as between AoStiff and PWV measurements ($r=0.75$, $P<0.0001$). GTN administration decreased mean arterial blood pressure by 4% (95% confidence interval: 2–8%, $P=0.002$) without significant changes in AoStiff and regional IWV. Local AoStiff is correlated with regional measurements and is not influenced by changes in arterial pressure because of systemic peripheral vasodilatation.

Keywords:
• Aorta
• Cardiovascular diseases
• Elasticity
• Peripheral resistance

Conclusion:
Although PWV and the AoStiff index are not strictly identical because of the inhomogeneous elastic properties of the arterial tree, both local and regional methods are well correlated, even in the presence of changes in arterial pressure due to systemic peripheral vasodilatation. In contrast to the regional methods, the local method assessed with the BI technique allows a differential analysis of the components of AoStiff (that is, resistance and distensibility). This technique could represent a useful tool for a more discriminating analysis of the effect of vasoactive drugs on the vasculature.

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Measurement of the local aortic stiffness by a non-invasive bioelectrical impedance technique

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**Abstract:**
Aortic stiffness measurement is well recognized as an independent predictor of cardiovascular mortality and morbidity. Recently, a simple method has been proposed for the evaluation of the local aortic stiffness (AoStiff) using a non-invasive bioelectrical impedance (BI) technique. This approach relies on a novel interpretation of the arterial stiffness where AoStiff is computed from the measurement of two new BI variables:
(1) the local aortic flow resistance (AoRes) exerted by the drag forces onto the flow;
(2) the local aortic wall distensibility (AoDist). Herein, we propose to detail and compare these three indices with the reference pulse wave velocity (PWV) measurement and the direct assessment of the aortic drag forces (DF) and distensibility (DS) obtained by the magnetic resonance imaging technique. Our results show a significant correlation between AoStiff and PWV (r = 0.79; P<0.0001; 120 patients at rest; mean age 44 ± 16 years), and also between AoRes and DF (r = 0.95; P = 0.0011) and between AoDist and DS (r = 0.93; P = 0.0022) on eight patients at rest (mean age 52 ± 19 years). These first results suggest that local aortic stiffness can be explored reliably by the BI technique.

**Keywords:**
• Aorta
• Cardiovascular diseases
• Drag
• Elasticity
• Flow
• Magnetic resonance

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Modeling and interpretation of the bioelectrical impedance signal for the determination of the local arterial stiffness

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**Purpose:**

Stiffness of the large arteries (e.g., aorta) plays an important role in the pathogenesis of cardiovascular diseases. To date, the reference method for the determination of regional arterial stiffness is the measurement of the carotid-femoral pulse wave velocity (PWV) by tonometric techniques. However, this method suffers from several drawbacks and it remains limited in clinical routine.

**Keywords:**

Artery, Cardiovascular diseases, Elasticity, Bioimpedance, Model

**Methods:**

In the present study, the authors propose a new method based on the analysis of bioelectrical impedance (BI) signals for the determination of the local arterial stiffness. They show, from a theoretical model, a novel interpretation of the BI signals and they establish the relationship between the variations in the BI signal and the kinetic energy of the blood flow in large arteries. From this model, BI signals are simulated in the thigh and compared to experimental BI data. Finally, from the model, they propose a new index (Ira) related to the properties of the large artery for the determination of the local arterial stiffness.

**Results:**

The results show a good correlation between the simulated and the experimental BI signals. The same variations for both of them with different characteristics for rigid and elastic arteries can be observed. The measurement of the Ira index on 20 subjects at rest (mean age of 44.16 yr) for the determination of the local aortic stiffness presents a significant correlation with the PWV reference method ($R^2=0.77; P<0.0001$ with the Spearman correlation coefficient and $\text{Ira}=4.25\times\text{PWV}+23.54$).

**Conclusion:**

All the results suggest that the theoretical model and the new index could give a reliable estimate of local arterial stiffness.

Received 23 January 2009; revised 20 July 2009; accepted for publication 21 July 2009; published 4 September 2009
**Abstract:**

The bioelectric impedance technique is a noninvasive method that provides the analysis of blood volume changes in the arteries. This is made possible by an interpretation of the impedance signal variations. In this paper, time and spatial variations of such impedance signals are studied on recordings made on limbs of 15 healthy subjects at rest. For that purpose, the scalogram of each signal has been computed and quantitative measures based on energies were determined. The results show that the signals are statistically time invariant on three anatomical segments of the limbs: pelvis, thigh, and calf. *p* value varies between 0.20 and 0.52 for the absolute energies computed on scalograms of signals recorded at 5 min intervals. Moreover, the analysis made on the two legs of each subject shows that the signals are spatial invariant on the three anatomical segments. *p* value varies between 0.0785 and 1.000 for the absolute energies computed on the scalograms of signals recorded simultaneously on the two legs. These conclusions will therefore help the clinicians in studying the temporal variations of physiological parameters on limbs with the impedance technique. Moreover, the results on the spatial invariance make possible the comparisons of these parameters with those given by other acquisition techniques.

**Keywords:**

- Artery
- Bioimpedance
- Impedance
- Limbs
- Noninvasive measurement
- Scalogram
- Spatial invariance
- Time invariance
- Time–frequency representation.

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